PROCEEDINGS
of the
ROYAL SOCIETY OF MEDICINE

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Section of Dermatology

President—H. MacCormac, C.B.E., M.D.

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[*February* 21, 1935]

Two Cases of Lymphogranuloma Inguinale.—H. MacCormac, C.B.E., M.D.

(I) J. C., a man, aged 25, first noticed a swelling of the right inguinal glands on Christmas Day 1934, and on December 31 the glands on the left side became similarly swollen. On January 9 he attended my clinic at the Middlesex Hospital, having marked swelling of the glands in both inguinal regions. The iliac glands were also distinctly palpable. The Wassermann reaction was negative. A diagnosis of lymphogranuloma inguinale was made and the patient was admitted into hospital. There, although the skin became red and the glands tender, the inflammation gradually subsided under treatment by rest and fomentations, and the patient was discharged on February 13. The Frei reaction was positive.

(II) The wife of the patient in Case I, a woman, aged 31, was seen one month ago. She had then an enlarged tender gland in the left groin and palpable iliac glands. The Frei reaction was positive. She is still in hospital undergoing treatment with solganol B, on the advice of Dr. Kleeberg, who saw both cases with me and kindly provided the Frei antigen. These two cases were also seen by Dr. H. Stannus, who confirmed the diagnosis.

Lymphogranuloma inguinale or poradenitis appears to have become much more prevalent recently in Europe : it has long been recognized in the Tropics as climatic bubo. The primary lesion may be herpetiform, a tiny sore, sometimes intra-urethral, inducing a discharge resembling gonorrhœa. There is no definite rash, although an eruption resembling erythema multiforme or nodosum may be observed. The characteristic feature is the adenopathy of the inguinal or inguino-cruro-iliac group of glands. The inguinal glands often break down with multiple fistulæ. This may be followed by elephantiasis of the penis, and in women by esthiomene, or the genito-ano-rectal syndrome, with elephantiasis and ulceration of the vulvæ and stricture of the rectum. We are, I believe, indebted to Dr. Stannus for recognizing the relationship of these diverse conditions, a relationship which has been proved by the Frei test.

Lymphogranuloma inguinale appears to be very uncommon in Great Britain, and the cases shown are the first in this country of a man and wife being simultaneously infected. One other case was exhibited at a meeting of the Section by Mr. J. E. R. McDonagh in 1924.[1] In a recent exhaustive investigation into its European distribution by Hellerström no British case is included, although every other country is fully represented. It is interesting, therefore, to speculate upon the appearance of two recent infections, not at a seaport, but in the centre of London. Possibly the invasion of the neighbourhood of the Middlesex Hospital by a colony of Cypriots may be the source of the disease.

[1] *Proceedings*, 1925, xviii (Sect. Derm., 35).

Genital Hypertrophy.—H. MacCormac, C.B.E., M.D.

J. T., aged 33. In 1931 chancre of scrotum : treated in Paris for two years. The Wassermann reaction is now completely negative.

This patient is shown because of the known relationship between lymphogranuloma inguinale and elephantiasis of the male pudenda. We may accept without reserve the original diagnosis of syphilis, as he was treated at the leading venereal hospital in Paris. The elephantiasis of the scrotum and penis developed eighteen months after completion of the treatment for syphilis. There are also pigmented warty areas on the left thigh and right knee which are probably independent.

As the Frei reaction persists long after infection it is still possible to determine whether originally a double infection with the spirochæte and the lymphogranuloma virus took place. Two days ago an intracutaneous injection of Frei antigen was made, the result of which is negative. The condition must therefore be regarded as syphilitic.

Discussion.—Dr. Hugh Stannus said that the Section was to be congratulated on seeing the President's first two cases, as they were perfectly typical examples of lymphogranuloma inguinale. Though such cases were not very commonly met with, or at least reported in this country, he thought it probable that a number had been missed in the past. If, ten years ago, a case with a non-suppurative adenitis, and yielding to simple treatment had been seen the observer would have been satisfied with the diagnosis of adenitis, and the real condition would not have been recognized.

The President had suggested that imported infection was responsible for the condition. Reference to the literature would show, however, that groups of cases had been described for a hundred years past, cases which, by their description, corresponded very definitely with lymphogranuloma inguinale. One of the best descriptions was that by Wallace, of Dublin. Of further interest was the fact that the present cases were partner cases.

There could not be much doubt that Dr. MacCormac's third case was one of lymphogranuloma inguinale infection. It was not uncommon in such cases in the tropics to find double infections.

Many people hesitated to agree that these cases of elephantiasis of the pudenda were due to a lymphogranuloma inguinale virus infection ; some believed that syphilis was a factor in the condition. There had, however, been recorded plenty of cases in which syphilis played no part. It was necessary to remember that the infection was a virus infection, and that the point of infection might be anywhere on the body. There had been excellent examples of primary infection on the tongue, with adenitis in the neck ; there were other cases, in children, in which the infection had been on the skin only. In women the primary lesion was most commonly on the vulva near the fourchette or the lower part of the posterior wall of the vagina. In China, in India, and elsewhere where pæderasty was practised, the initial lesion was on the anal margin. In those cases in which the initial lesion was in the neighbourhood of the perineum, the inguinal glands were commonly not affected, while the glands which drained that area of skin namely those round the rectum, the pararectal glands, were involved. It was in these cases that blocking of the lymphatics in the pelvis occurred, with the production of elephantiasis of the vulva and anal region and infiltration round the rectum, which went on to rectal stricture.

He thought it would be recognized, in the future, that every case of "inflammatory stricture of the rectum" was due to a lymphogranuloma inguinale virus infection. This stricture of the rectum was very common in China, there were many cases in Africa, and in other areas where climatic bubo was common.

The condition of the skin of the patient's leg and buttocks was typical ; it occurred in many cases of elephantiasis of the vulva, and in men it was not uncommon in association with infections about the anus and with rectal stricture. In rectal stricture it was common to see multiple fistulæ develop about the anus, just as one saw happen in the groin. Lipiodol injection gave a beautiful picture of the often complicated series of fistulæ.

The Frei reaction he (Dr. Stannus) regarded as absolutely specific, always having regard to certain conditions. Some French authors had cast doubt on this point, but every case published in which doubt had arisen the failure could be explained. It was known that the

Frei reaction might not be positive during active syphilis; also it might be negative during menstruation, in fact, since it was an allergic reaction, it might be interfered with, as other allergic infection might be, by certain conditions. The reaction probably lasted throughout life, but it was not yet certain. In Dr. MacCormac's case the skin reaction might be regarded as doubtful; it had certain characters which were suggestive, as Frei himself had pointed out, it was much easier to feel the lesion than to see it, and the sensation was very characteristic, that of a dome-shaped swelling. Hence, he would say that this was a doubtful case. In this man the condition might be due to some other cause than a lymphogranuloma inguinale infection, and before declaring the reaction to be negative he thought it would be necessary to test with several antigens. Probably there were different strains of the virus, one strain of antigen might give a positive reaction when another strain would not do so.

He felt, however, that this was probably a case of elephantoid condition due to granuloma inguinale virus.

Another point about this patient was that he had the very typical little peri-anal growths which were mentioned by Hugnier in 1848 when he originally described esthiomene. If this man had not already some perirectal infiltration, he (the speaker) would not be surprised if he developed a rectal stricture. It would be interesting to have later information upon this point.

Dr. P. H. MANSON-BAHR said that he had been most interested to see in the second case shown by the President an undoubted instance of lymphogranuloma, or what used to be called "climatic bubo," in the female. The occurrence of the typical bubo in the female sex had not, so far as he knew, been hitherto described in the tropics. But whether the condition in the third case could justly be described as clinically the result of this disease, he was by no means sure. He had never seen anything like it before and he had been observing cases of "climatic bubo" in Lascars, Chinese, Japanese, Negroes, and Europeans, arriving in this country for the last twenty-five years, and he had also seen the disease as it occurred in natives in the tropics itself, but he had never observed the elephantoid condition of the penis, the corrugated appearance of the scrotum, the infiltration of the skin and subcutaneous tissues, with the formation of almost cartilaginous plaques, as in this peculiar case. He deprecated the tendency to dub every anomalous granulomatous affection of the groins as "lymphogranuloma inguinale" without some more exhaustive and adequate proof, just because this term had become popular and because this disease was in the medical limelight at the present time.

Dr. W. J. O'DONOVAN said he was not sure that the conditions in the third case were typical of lymphogranuloma. He himself and many members must often, on more familiar grounds, have regarded clinical pictures as typical, and yet the development of the cases or further laboratory investigation had shown that a characteristic appearance did not imply a certain recognition of the underlying pathological process. In one sense, to say that the condition was typical imposed a barrier to further investigation. In spite of what he himself had demurred to, he would suggest that the condition on the left thigh was typical of leprosy, but he would like to suspend judgment on this particular case until further laboratory investigation had thrown light on to the true nature of these raised nodes of infiltration.

Dr. STANNUS, referring to the remarks of Dr. Manson-Bahr, said that the cases of climatic bubo which came under observation at the Hospital for Tropical Diseases, were cases which had contracted their infections often but a few weeks before, they were early cases, they came under care and became better quickly, and so did not develop the serious conditions, which were not uncommon in tropical countries. The question of how far the infiltration proceeded was largely one of time. In the President's third case, the whole of the glands of the groin, the crural glands, and the iliac glands were a solid mass of infiltration.

With regard to the point raised by Dr. O'Donovan concerning the use of the word "typical" he suggested that most clinicians carried in their minds pictures of conditions and diseases which were types, and he contended that this was a normal process of reasoning.

Dr. W. J. O'DONOVAN said he confessed that he had often fallen into the pit of error through accepting a typical appearance as being conclusive. He understood that the whole history of the case, the clinical appearance, the development and laboratory findings, were all essential before a decisive judgment was passed on such cases as were brought before the Section.

Cutaneous Gummata with Cardiovascular Changes.—H. MacCormac, C.B.E., M.D.

J. A., a man, aged 71, contracted a sore and bubo in Egypt forty-eight years ago ; the bubo was opened and dressed, but no other treatment was given. He has had an unusually healthy life up to the present time, doing strenuous work —as a porter—which entails carrying heavy weights, coal, etc., up three flights of stairs. His wife is alive and said to be healthy and there are two healthy sons.

The patient is able to fix the date of his original infection accurately, as it coincided with Queen Victoria's Jubilee ; he has thus remained a latent syphilitic in robust health until our present King's Jubilee year, when he developed a gumma on the arm.

Appearances are apt to be deceptive, and Dr. Evan Bedford, to whom I referred the patient, reports as follows :—

"*Diagnosis.*—Arteriosclerosis, hypertension ; syphilitic aortitis with general dilatation of the aorta and stenosis of the innominate orifice ; aortic incompetence and moderate enlargement of the heart to the left.

On examination.—Pulse regular ; rate 80. The right radial and right carotid pulses are of small volume and anacrotic. Arteries, moderately thickened. Blood-pressure 220/90 mm. Apex-beat displaced to the left ; systolic and diastolic aortic murmurs.

Radioscopy : General dilatation of the aorta involving especially the descending arch, and characteristic of syphilitic aortitis. Moderate enlargement of heart.

Electrocardiogram : Shows inversion of T in lead I and indicates myocardial impairment. There are no signs of congestive failure.

The remarkable feature of this case is the absence of any severe symptoms, in spite of considerable cardio-aortic damage, and the fact that he has been able to work as a porter so long. The latent period of forty-eight years is twice as long as is usual in the case of aortitis.

Syphilitic Glossitis in a Woman.—H. MacCormac, C.B.E., M.D.

Miss J. M., aged 53. No history obtained of original infection which, however, may be presumed to have occurred during the years of the Great War. First seen one year ago, when she had a superficial glossitis resembling lichen planus. The Wassermann reaction was then negative. As the condition was becoming progressively worse she returned to the Middlesex Hospital recently. It was then noted that she had typical syphilitic glossitis over the anterior third of the tongue, with ulceration near the tip and on the right side. The Wassermann reaction is now positive. Following three injections of novarsenobillon there has been a marked improvement.

The patient is a non-smoker—an interesting point, because smoking, and especially pipe-smoking, is an important causal factor in the relatively common presence of buccal leucoplakia in men with old-standing syphilis. For this reason both specific leucoplakia and cancer of the tongue are rare in the female sex.

In this patient a pre-malignant lesion exists and it may be necessary, as a precautionary measure, to use radium.

Cutaneous Gumma Persisting in spite of Treatment.—H. MacCormac, C.B.E., M.D.

A. S., a man, aged 46. No history of specific infection or gonorrhœa. In March 1931 a gumma developed on the right arm. The patient was then under the care of Dr. J. Green ; as he was not making progress he was referred to the Middlesex Hospital. When seen by me in June 1932 he presented a typical and extensive gumma on the right arm. The Wassermann reaction was strongly positive. Intensive treatment—arsenic and bismuth—has been carried out for two years but

although the Wassermann reaction became negative and remains negative, the gumma has never healed completely. This failure of a gumma to respond to treatment is most unusual.

It should be pointed out that this patient has not been treated with mercury and it is possible that a course of mercurial injections will succeed where bismuth and arsenic have failed.

Discussion.—Dr. E. MALLAM asked whether the President had given iodide of potassium in this case. If not, he (the speaker) thought that large doses of that drug would very likely clear the condition up. He personally would not hesitate to use half an ounce or more a day.

Dr. E. STOLKIND said that possibly microscopical examination of sections of the skin might reveal the presence of a tuberculous lesion. The treatment of the general health might influence the recovery.

Dr. J. A. DRAKE said that it was very unusual to see a gumma lead to contraction, and he did not recall a case with such marked retraction as was seen here.

Dr. C. H. WHITTLE, referring to the possibility of tuberculosis in this case, said he had now under treatment a girl who presented a similar lesion, on the arm. It was tuberculous, and had produced a scar and contracture similar to those in this case.

Dr. P. C. P. INGRAM asked how many grammes of arsenobenzol this patient had had during the last two years. He did not seem to be the kind of man who could stand very much.

The PRESIDENT (in reply) said that the condition was typically syphilitic; he did not think it was tuberculous or complicated by tuberculosis. Had both diseases—tuberculosis and syphilis—been present, progressive destruction would have ensued, as was well known in the association of tuberculosis and syphilis in the same patient. The fixation of the elbow was, he thought, due to the posture in which the arms had been carried. The total amount of novarsenobillon given was 5·7 grm.; this was well tolerated, although simple jaundice had subsequently developed.

Dr. W. J. O'DONOVAN said, with regard to the jaundice, that this might be an early case of toxic hepatitis and, should the patient visit another clinic and receive salvarsan-therapy, he might be in danger of an attack of acute yellow atrophy of the liver which had a mortality rate of one-in-three. [The PRESIDENT: I often give salvarsan to a patient who has had jaundice and I have never seen any ill result. In fact, some physicians believe in giving more salvarsan if there is jaundice, as they consider that to be a syphilitic manifestation in the liver.] He (Dr. O'Donovan) had known a number of cases in which the patients had died of jaundice, due to liver-atrophy after salvarsan-therapy, and he would like to know how in tertiary cases in which jaundice developed after salvarsan treatment, a diagnosis of syphilitic jaundice was maintained.

Cutaneous Gumma.—ERNEST MALLAM, M.D.

W. G., aged 52.

Diagnosis.—Tertiary syphilis involving the sternum and skin, heart, liver, ? pleura, and central nervous system.

Previous history.—Unmarried. Was a builder's labourer until the time of the Great War. Joined up in 1916. Invalided with painless abscesses on the front of the chest in 1917. Treated for these in military hospitals for about a year and then discharged.

Admitted to Radcliffe Infirmary, May 1934, with a history of two months' ascites, for which he had been tapped twice before I saw him.

May 29, 1934: Ten and a half pints of clear yellow fluid, showing endothelial cells, withdrawn from the abdomen.

June 1, 1934: A further eight pints of fluid drawn off. Nothing abnormal could be felt in the abdomen after tapping. The sigma reaction was strongly positive. Vigorous treatment with potassium iodide and mercury soon cured the ascites.

In June 1934 patient also exhibited: (1) Typical syphilitic scars over the sternum; (2) aortic disease: heart enlarged; to-and-fro murmur; water-hammer pulse; (3) tabes; pupils not reacting; right smaller than left; knee- and ankle-jerks absent; right plantar reflex flexor; left extensor; no Rombergism.

Signs of trouble at the base of the right thorax, can now be seen in skiagrams.

The genito-urinary and other systems appear to have escaped injury so far.

The PRESIDENT said that an interesting point which Dr. Mallam had not emphasized was the association of tabes and cutaneous gummata—a very rare combination.

Superficial Ulcers in Tertiary Syphilis.—HENRY CORSI, F.R.C.S.

Mrs. Lily E., aged 34, is the youngest of a family of twelve brothers and sisters. The other eleven are all well and married. Father died aged 76; mother killed in air-raid. Patient has been married twice. She has had no pregnancies.

On January 29, 1935, she came to St. Bartholomew's Hospital, complaining of superficial ulcers from one to three cm. in diameter. There were two under the fold of the right breast, one on the right flank, and one in the right popliteal space. In addition there was an eroded papule at the side of the left nostril. She was seen by Dr. A. C. Roxburgh who advised Wassermann and Sigma tests. The reactions proved strongly positive. When seen on February 5 she had been applying brilliant-green, 1%, for a week, without any benefit whatever. Novarsenobillon, 0·3, was given; a marked sudden improvement was noticed by the patient four days later. On February 12 novarsenobillon, 0·45, was given and further marked improvement followed, with regard both to the ulcers and to the patient's general appearance.

Eight years ago she suffered from similar ulcers and was an in-patient at East Dulwich Hospital for eight weeks, the ulcers being very slow to heal. The scars of these ulcers are visible.

? Primary Lesion on Eyelid.—GODFREY BAMBER, M.D.

I. M., single, aged 23. At Christmas-time a splash of hot fat fell on the eyelid. The injury was trivial, but about two weeks later a swelling developed at the site.

When first seen by me two weeks ago there was a large firm raised flattish papule on the right upper lid. In the middle of the lesion was a shallow ulcer, and the surface of the outer part was irregular in places. On palpation, the lesion felt like a disc of cartilage buried under the epidermis. No enlarged satellite gland was found.

No spirochætes were found either on dark-ground examination or in stained slides. The Wassermann reaction at the time was negative. Cultures gave a growth of *Staphylococcus aureus*.

The lesion may be either an extragenital sore or a staphylococcal granuloma.

Discussion.—Dr. L. FORMAN suggested the possibility of a primary tuberculous chancre of the skin. He had seen a girl aged 15 with what was thought to be a syphilitic chancre of the chin, characterized by a localized hard infiltration of the regional lymphatic glands. The glands eventually broke down and tubercle bacilli were demonstrated. The patient had a tuberculous fiancé.

Dr. A. M. H. GRAY asked what the experience of members was with regard to primary syphilitic lesions affecting the eyelids; was it not the rule to see much local œdema in those cases? In the few cases of the kind which he had seen there had been a good deal of red infiltration round the lesion.

Dr. W. J. O'DONOVAN said that Dr. Gray's remark was very pertinent, i.e. that in cases of primary sore of the orbital skin there was a great deal of œdema. The possibility of tuberculosis and of staphylococcal granuloma had been suggested, and he would add another.

He had been occasionally puzzled in such conditions of localized granuloma by mycotic infections; in such cases the assistance of the laboratory seemed to be essential in order to arrive at a correct diagnosis.

Dr. BAMBER (in reply) said that this patient developed the lesion a fortnight before he saw her, and she said that the swelling had been almost sufficient to close the eye.

With regard to the suggestion that it might be tuberculous, he did not think the ulceration was sufficiently deep for that, considering the time factor. He had not seen her for a week, and there was now ulceration in several places, which was unlike the behaviour of the ordinary primary sore. He would bring the note of the condition up to date.

POSTSCRIPT.—On February 26, 1935, the Wassermann reaction in the blood was again negative.

? Gumma of Scrotum.—L. FORMAN, M.D.

Male, aged 40.

Circinate late secondary syphilide of the scrotum. Eruption, with considerable itching, present for four weeks. Superficially ulcerated and excoriated papules arranged in a circinate manner on the scrotum; also papules around the anus. Wassermann reaction positive (+ +).

Gumma of Neck and Scalp.—L. FORMAN, M.D.

Female, aged 55. Serpiginous superficial tertiary syphilide; Two years' history. Serpiginous infiltrated area on the right side of the neck behind the ear and the temple. Patient has had four children and one miscarriage. Blood-Wassermann reaction + − ; Kahn reaction ++++.

Large Papular Syphilide.—R. T. BRAIN, M.D., and A. J. KING, F.R.C.S.

A. D., aged 37, labourer.

Three weeks' history of sore on penis and rash; said to have appeared at the same time. Sore healed in one week; rash persisted. No other symptoms.

Previous gonorrhœa, fourteen years ago. Exposure six weeks and six months ago.

On examination.—Widespread papular rash on trunk, face and limbs. Œdema and induration of prepuce. Generalized adenopathy, especially of epicondylars and right anterior and posterior triangles of neck. Superficial ulceration of both tonsils.

Dark-ground examination: Spirochætes not found in serum from papules; several examinations.

Serum reactions (19.2.35): Wassermann, positive (+ +); Kahn, strongly positive.

Superficial Verrucose Gumma.—R. T. BRAIN, M.D., and A. J. KING, F.R.C.S.

H. C. H., aged 44.

Three months' history of ulcer at left angle of mouth; began as a pimple; this has discharged a little, and is slightly painful at times; it has been treated with local applications.

Patient denies having had previous venereal disease. Wife is well, six months pregnant; one child aged 7, healthy; no miscarriages.

On examination.—Infiltrated mass at left angle of mouth. Skin surface shows irregular verrucose projection with central atrophic area. Some leucoplakia on mucous aspect. No enlargement of lymphatic glands in drainage area.

Serum reactions (18.2.35): Wassermann, positive (+ +); Kahn, strongly positive.

Is this diagnosis agreed upon? Because in spite of the result of the Wassermann test, the warty condition also suggests tuberculosis or a chronic septic granuloma.

Discussion.—Dr. ANWYL-DAVIES said that although there might be an alternative diagnosis concerning the ulcer at the angle of the mouth, the marked glossitis of the tongue would, he thought, be described by most observers as syphilitic.

Dr. P. C. P. INGRAM said that he had had a case similar in appearance and site, a few years ago. The condition had cleared up rapidly and completely under treatment by arsenobenzol and bismuth.

Subcutaneous Gummata.—R. T. BRAIN, M.D., and A. J. KING, F.R.C.S.

R. B., aged 54. Labourer.

Two years ago an iron gate fell on to his left leg; later, a swelling appeared on the left shin; this persisted and increased in size. Six months ago the swelling began to "break up" and three sores developed, these were slightly painful at times.

Sore on penis thirty-four years ago, treated with local applications only.

Wife alive and well; one healthy son; no miscarriages.

On examination.—Circular punched-out ulcerated area on subcutaneous surface of left tibia, about 3½ in. below the line of the knee-joint. Regular margin: clean granulating base with a small sinus, at the anterior extremity, leading down to bone. Two other recently healed smaller areas of ulceration above the main lesion. Œdema of the subcutaneous tissues distal to these areas.

Serum reactions (11.2.35): Wassermann positive (++); Kahn strongly positive.

Treatment (14.1.35 to 7.2.35): Eight injections of bismuth oxychloride 0·2 grm. (total = 1·6 grm.) by the intramuscular route; potassium iodide by mouth—not exceeding 45 gr. daily.

Section of Epidemiology and State Medicine

President—J. D. ROLLESTON, M.D.

[*February 22, 1935*]

DISCUSSION ON THE PROBLEMS OF RURAL WATER SUPPLIES

Lieutenant-Colonel C. H. H. Harold (*Director of Water Examination, Metropolitan Water Board*) : For upwards of twenty years it has fallen to my lot to give advice on and to supervise water supplies of a rural type in areas extending from the Punjab to Turkestan, and in the Aldershot and Southern Commands.

When considering this problem in a broad way, it is seen that the question is of universal application to all parts of the world, and its solution is governed by two main factors, rainfall and the availability of sources of supply. It is of interest to note that in this country widespread publicity has been given to a certain scheme designed to deal with this defect in rural areas by one standardized method, e.g. the laying of trunk mains.

Many years ago, a deep impression was made upon me by the fact that it proved cheaper to instal a tube well system in conjunction with existing mains, than to link these up with a neighbouring supply. Later, this view was substantiated in the case of a large scattered cantonment, when it proved more economical to put down two or more bores with shorter mains, which might eventually be joined, rather than to lay full trunk mains from a central source.

If the big idea method of solving the difficulty were the only one, then the problem would be simple, resolving itself into a matter of money and more money. The next question, then, is " Who is going to pay for it, and what return could be expected for such an outlay ? " It was of interest to learn during a recent visit to France, which has also become more " water-conscious," that a proportion of profits derived from taxes from the *pari-mutuel* are set on one side for the subsidization of rural supplies. It may be said that such discussions are outside the province of doctors, but it is necessary that doctors should have some basal knowledge of chemistry, geology, engineering, and finance to enable them to exercise discrimination in formulating, or discussing, schemes. Conversely, the engineer of to-day is fully alive to all general details appertaining to purity.

There is no doubt that the question demands every consideration, since, according to certain water-engineers who have spent their lives in this service, upwards of six million people are without a reasonable water supply, in spite of the fact that it is possible to provide 80% of these with piped water at a reasonable cost.

There is undoubtedly a steady flow of people from the country to the towns, and it is not surprising to learn that, according to certain authorities, the general health in the country is worse than in the large towns. Difficulties regarding housing, sanitation, medical care, and food and water prevail, and the incidence of enteric fever in 1933 was $0\cdot04$ per million for England and Wales, compared with $0\cdot06$ for Rural Areas.

In rural areas all milk of reasonable quality is collected and dispatched to the large organizations in the cities, and in one town in the heart of the finest agricultural country in England, considerable difficulty was experienced in making a suitable contract for the supply of good milk to the troops, since only the inferior and doubtful milk is available for local consumption, and in certain villages meat is only procurable when a beast is slaughtered.

Intimately bound up with rural England is one of Britain's greatest industries, agriculture, with an estimated annual earning capacity of £220,000,000 sterling. The number of people registered in this employment is 687,700, and it is considered that an additional 2,000,000 are really needed. Recently there has been a decrease of 21,500 male and 6,400 female workers, all of whom are specialists in their craft. Under these conditions, it says much for the basic soundness of the industry that Britain still stands supreme as the breeding place of pedigree cattle and sheep.

Our Prime Minister has recently indicated that it is the aim of the Government to make a big drive in the development of this industry, thereby providing employment for larger numbers and reducing national expenditure on foreign produce.

We, as medical men, also know that from this nursery human additions pass to refresh urban populations, and from it a large proportion of healthy stock is derived for the maintenance of our armed forces. Lastly, it is to these refuges that many retire for recreation and rest after lives of arduous toil.

Commercial concerns accept the necessity for expenditure on water, but when in the Southern Command, where much time was spent on tours, meeting farmers on War Department lands, in camp areas, etc., one could not help being struck by the fact that the majority of rural dwellers regard the supply of water as a gift from above, like the sunshine, the possible exceptions being those connected with milk factories, etc., who have developed a more industrialized outlook. The others endure conditions of drought much in the same way as they endure foot-and-mouth-disease, or blight, and when shortages abate, revert to their local shallow well supplies. Such people would resent the imposition of a water-rate.

The situation has undoubtedly been complicated by the rapid development of transportation, bringing rural areas within a few minutes' reach of towns, and many houses have been built during a cycle of wet years. The failure of inadequate supplies has resulted in urgent requests to local authorities, who, in abnormal periods, can do little to alleviate this shortage. This and many other difficulties associated with extensive building operations call for a keener watchfulness in the future.

If we trace the scheme of things back, we find that man was originally a river-dweller, and from this source he derived water for himself and his flock, and food, in the way of fish, while the river also provided a ready means of transport. Later, his migrations were influenced by the availability of springs, and the permanence of wells and dew-ponds. Hence, traditionally, from man's point of view, the river is primarily a source of water-supply, secondly a means of transport, and lastly an outlet for normal drainage of the area.

As previously indicated, rural supplies must depend upon local resources, and if their integrity is to be maintained, these must be zealously safeguarded. The extension of building operations, the making of impervious roads, increased drainage and the training of rivers, although excellent and necessary in their way, all deprive the soil of its wonted moisture, leading to a reduction in subsoil water. It is held by some, that spread over a large area, such losses are negligible compared with the volume of underground reserves. Still, the changed appearance of the countryside and the confluence of proofed areas are striking and are increasing day by day.

It is possible that those of us who have dealt with water problems in countries where irrigation is practised, and have seen rises of the water table leading to a change of arable land to a sick and waterlogged condition, may be unduly impressed regarding the potentialities of increases or decreases in surface water.

Furthermore, the increasing output of sewage effluents exercises a disturbing influence upon the purity of our rivers.

Things would, however, have been much worse were it not for the more efficient purification of sewage effluents and the control exercised by the various conservancy boards.   It is very difficult to convey to the lay mind that there is a vast difference between a good sewage effluent and an ordinary river water, and however good an effluent may be, if it is to attain a condition comparable with that of a reasonable river water, the breaking down of its contained sewage components by biological action must be continued in the river.

To accomplish this, effluents require dilution with eight times their volume of good river water.   Yet this summer has seen virile rivers staggering under a load of sewage pollution, indeed, in many places the very waters themselves have been displaced by such effluents.   No ordinary person expects a biological sewage plant to work beyond its capacity, and similar consideration should be given to a river. Indications point to the fact that rivers may deal satisfactorily with relatively huge volumes of effluents if they receive them in small additions, each succeeding addition being diluted and activated by the seeded water coming down-stream.   Under such conditions the vitality of the river is not seriously impaired, whereas the impact imparted by a massed introduction of effluent may cause an intense degradation of the river, from which it may not recover.

For these and other reasons, which will be commented upon later, the inclusion of a strong medical and chemical opinion on all special committees dealing with these matters is strongly urged.   By such means it is hoped that conditions resulting from certain legacies of the past may not be re-created, or even perpetuated.

It is now considered opportune to comment upon the steps taken by the Government which have for their objective the permanent relief of these deficiencies.   It is submitted that the measures call for unqualified approval, although if we are to believe all that is said, no Government in power has ever fulfilled its obligations.

The Ministry of Health has very wisely refused to be stampeded into hasty legislation, and one of the chief proposals is the institution of a hydro-geological survey.   That such is a useful measure cannot be doubted, when it is realized that during the height of the drought last summer, a survey of possible sources within the area operated by the Metropolitan Water Board led to the augmentation of the supply by several million gallons per day, without in any way depleting its own or surrounding reserves.

The next is the provision of £1,000,000 for expenditure on local schemes, and this sum, if expended on the small and most needy areas, will, in view of the size and cost of such undertakings, be a very material help.   It is extremely difficult to bring home to people that, in these poor areas, the cost of an extra few yards of mains, or even the part-time employment of a single man, is a definite burden and has to be most carefully considered.

By such legislation, it devolves upon local authorities with all the knowledge of the requirements and resources of the area, to put forward their local scheme, which will not, as a rule, involve participation in a large undertaking.   As a result, all parties have a personal interest in its development, financially and otherwise.

To the members of this Section a paper written by Mr. R. G. Hetherington, Chief Engineering Inspector of the Ministry of Health, is strongly commended.   This paper, read before the British Waterworks Association in November last, succinctly states the main points of the case, the chief being that water must be sought where Nature has placed it, also that the controlling expense in the supply of water is distribution.   Among other important details this officer lays great stress upon the value of good wells as the great stand-by of rural sources.

When reviewing means of utilization, the scientific and mechanical advances during the last few years strike one as being remarkable, and visits are suggested to

two installations, one at Henley and the other at Princes Risborough, as exemplifying models of mechanical control. It is uncanny and intriguing to stand alone in an engine-house and note that as water-pressure falls in the mains, the engines start up automatically, chlorination and softening apparatus operate, and all cut out when the required pressure is attained.

These auto-pneumatic systems operate without reservoirs, may serve as boosters, and may be applied to any source. Mechanical filtration and softening may also be incorporated in the system. The plants only require occasional visits, and a warning signal may be fitted to attract attention in event of a mechanical breakdown.

The sources of energy may be steam, petrol, oil, or electricity, and such adaptability permits of universal employment. Mr. Worger, a former District Engineer and Officer of the Metropolitan Water Board, has dedicated his years of retirement to the study of this problem, and to him I am indebted for much information. He has in mind the standardization of these power units in regional areas, and in the event of a breakdown, proposes stand-by motor trolley units. Naturally, such suggestions make a special appeal to people with an Army training, but England is not a country in which standardization finds ready acceptance.

For all general purposes there are available a host of mechanical devices—rams, hoists, air-lift pumps—which do not call for special observations here.

Now follows the consideration of various sources of supply, and the underlying principles affecting them can be applied in any part of the globe.

The receipt of a sample of water at the laboratory, with a request for examination and report regarding its suitability, is of almost daily occurrence. It is necessary to reiterate continually that random sampling is of little use in arriving at an opinion as to the suitability of a supply, and that no amount of laboratory work can replace inspection of the environs of its place of origin.

After inspection, laboratory decisions may lead to the rejection of about 17% of provisionally selected sources. In India, without inspection, the bacteriological results given by good wells may be entirely misleading. However, the laboratory is the controlling influence in the operation of existing undertakings and is indispensable in the detection of hidden pollutions.

Rivers.—Such sources are either taken into regular use, or may be only supplementary, when local wells, etc., fail, though at such times they are usually greatly depleted and probably excessively polluted. Their inclusion is often fraught with considerable difficulties, in that they are prone to sudden variations in their quality, resulting from flood, pollution, algal growths, and other agencies. Abroad, may be added as troubles, clay, mica, and glacial silt, a trinity to try the heart of the stoutest water-purifier. The utilization of river-water necessitates sedimentation, possibly aided by a coagulant, followed by filtration and disinfection. This entails supervision, labour, plant—in other words, the expenditure of money. When exploring methods of exploiting these sources, the use of a sedimentation basin, which is filled when the stream is clear, is frequently found. Another expedient is the driving of galleries parallel to the river into which water from the land and river seep. This device is used in many places, for example, in Bermuda; I saw it recently at Nancy. It is a method adopted along sea-coasts, to tap sweet water finding its way to the sea.

At times of low water, excavations may be made in the river-bed alongside the bank, inside which shuttering of sheet iron, or wood, is carried down on piles to exclude the superficial flow of the river. From such wells clear water may be drawn. On the same principle, the water at Ambala is drawn from a well sunk in an expanse of dry river bed, and needs no special clarification.

In rivers with gravel beds, the inlet may be encased in a cage buried some feet down in the gravel. Such a device often succeeds in tapping spring water flowing

into the river from below, and frequently ensures the delivery of comparatively clear water, even in times of flood.

It may be advantageous to consider briefly one or two improvised methods, which have been found useful in an emergency and require a minimum of attention.

After a selection of a suitable site on a river bank to allow for a slight fall, a syphon is introduced, or a small channel cut to three sedimentation pits, communicating in series. A simple constant-level alum tank, operated by a float, feeds into No. 1 pit, and the system may be made to operate on the draw-and-fill principle. Another simple modification of the Puech-Chabal system may be arranged by connecting up four pits in series. No. 1 is filled with graded stones, No. 2 with shingle, No. 3 with shingle and sand, and the last is used as a draw well. In both these methods, water may be drawn from a shuttered well, previously described, and as a finishing process, a barrel clarifier may be included.

A reasonably clarified water for domestic purposes may frequently be obtained by using a floating hogshead with a perforated end. It is half-filled with shingle and sand, and placed in an excavation near the bank. It should be anchored so as not to touch bottom, and water is drawn by bucket from the top as required.

In all improvised measures, a length of hose, an ordinary field-pump and a few horse-troughs can be put to a useful purpose.

An inexpensive and most useful appliance is the Norton's tube, which can be used in the vicinity of rivers, or where a reasonably high subsoil water level is known to exist. Its utility as the means of obtaining a good, and even permanent, water supply has been established by the experience of 20 years, or more. In early days it was used for expeditionary forces, later for the rapid establishment of cholera and other camps, and afterwards as a permanent installation for bungalows and barracks. These tubes can be driven in a very short time and, when protected by a grouted platform leading to a runnel, have been known to supply water of the highest bacteriological purity. In one cantonment a well-constructed deep well frequently delivered water containing coliform organisms in $0 \cdot 1$ c.c., or less, and a Norton's tube within a few yards gave water negative for *B. coli* in 100 c.c.

It may appear strange to hear a staunch advocate of the selection of the best sources of supply and the utilization of water of the highest degree of purity, discussing the possible inclusion of shallow sources. Still, water derived from selected gravel beds and taken into the London supply yields 70% of samples free from typical *B. coli* in 100 c.c., with negligible colony counts, and of good chemical quality. If the gathering ground affords a reasonable degree of filtration and is safeguarded from obvious pollution, a device which has proved its worth in the gravest times merits consideration, and shallow sources are not to be despised.

We now pass on to consider wells and springs, which offer a most fascinating study. From time immemorial wells have been the subject of veneration, as givers of life, and in Japan and India shrines are to be found in their immediate vicinity, to which offerings are made. Holy men frequently establish themselves in such situations, which, like the village pump, are places of assembly. In this country, beliefs in the efficacy of certain holy wells and wishing-wells are not without adherents.

It is impossible to bring to mind the number of wells visited in various parts of the world, but included in their number are some attributed to Alexander and the Great Moghul.

In the case of the former, the site of the original town, or village, is only represented by an eminence, and in the latter the elephant-troughs are still to be seen. Such wells owe their permanence to the attractive qualities of their water, or possibly because the chances of finding water elsewhere in the locality are extremely remote. Of historical interest is the Karez, which is found in East Persia and Baluchistan, and is probably the oldest and most primitive of water supply systems. Briefly, it consists of a circular tunnel conveying water from an outcrop under the hills to the lower parts of the valley where the town is sited.

The Karez is lined with loose round river stones wedged in with a mallet. The system may be many miles in length, and at 80-yard intervals an air-shaft connects the channel with the open air. This shaft allows access for small boys, who carry out the necessary repairs resulting from roof falls and the accumulation of débris. The tools used are limited to a rope, a plummet, a basket, a mallet and a kind of mattock. During its course across the valley, surface water seeps into the Karez between the loose stones. The volume of water is frequently considerable and is used for irrigation. The water is not common property, but the rights of use are purchasable from the owner.

Springs issuing from the hillside, or rock face, require special protection, which is usually afforded by making a "diggi" and keying the lateral walls into the hillside. It is a good principle to oppose all suggestions regarding works to improve the flow, lest the spring disappear entirely. Since many of these result from faults, the conservation of the area must be rigidly imposed, although, as in the case of the Khyber supply, the gathering ground may be too far distant to be identified.

On one occasion, when the purity of a very important spring of this nature was being investigated, it was found that the hillside roofing the spring had been taken into use as a burial ground.

Even in the most arid and rocky areas, good water is frequently located by sinking relatively shallow shafts high up a valley at the head of a ravine, from whence water may be led away before it is lost under moraine, or by faulting of the subjacent strata. The water in these situations is often of considerable purity but tends to be somewhat hard.

The next and most important supply is the deep well. This needs no special description, except that it should be covered and fitted with suitable lifting gear, and afforded good protection from surface and other pollution.

Artesian wells are frequently met with, the well at Swindon being a notable example, but it is not possible to forecast with any degree of accuracy where such conditions will be found. During the height of the recent drought, a bore at Sundridge, in the Kent area, delivered water above ground level.

Earlier in the paper comments were made on the pollution of rivers, and certain points in connexion with superficial and deep waters seem to merit amplification.

The position of certain archæological finds lends support to the view that during the last thousand years, or more, a gradual fall has occurred in the water table in Great Britain. In certain areas, such as the London basin, this is very definite and results from excessive pumping from the chalk. This deposit is calculated to cover a combined area of 13,000 square miles, comprising 7,000 miles superficial chalk and 6,000 miles of deep formation, and, at present, it is drawn upon for a yield of 250-300 million gallons per day. Approximately, one-sixth of this amount is pumped by the Metropolitan Water Board, and the chalk provides 15-18% of the London water supply. Most of the water flows in fissures, which tend to enlarge under the influence of pumping and as a result of the solution of the chalk. The more vigorously this source of supply is drawn upon, the greater the possibility of gaining communication with channels carrying impure water. Consequently a constant watch must be kept over the chemical and bacteriological analyses furnished by such a supply, and any variation must be regarded with the gravest suspicion, since the Kent wells, which are of undoubted purity, deliver straight into supply without chemical treatment. Generally speaking, there is a great feeling of security in having a well some 200 feet deep, or more, and in the case of a good well this confidence is not misplaced. It may be of interest to cite certain records exemplifying the need of supervision.

An excellent illustration of chalk well pollution is to be found in the proceedings of the Epidemiological Section of this Society, 1908, vol. 1, p. 191 (Richards and Brincker). In this paper mention is made of the outbreaks of enteric fever due to deep well pollution at Caterham, resulting in 352 cases and 21 deaths, Worthing, 1,817 cases, 168 deaths, and

Newport, Isle of Wight, 436 cases with 42 deaths. The particular well which was discussed in this paper was 200 feet deep and the water derived from it showed signs of intermittent cloudiness. The origin of this was traced to a depression denuded of clay two miles south of the well, which acted as a soakaway, receiving storm water from an institution and the area around. By the use of salt and test microbes a direct communication was traced to this spot in about thirty to seventy hours.

That this pollution was direct, and not due to general pollution of the chalk, is indicated by the fact that an adjacent well operated by the Metropolitan Water Board was unaffected.

There is a close correlation between the chalk and our rivers, and an increased flow in the river is usually associated with a rise in water level of wells. This does not mean that there is a connexion between the river and the adjacent wells, but that both are fed by the same area in the chalk. The break of the drought was associated with a much slower rise in the Kent wells than in those in the Northern District, which have not the same bacteriological purity and are used for augmenting the flow of the New River, and improving its chemical quality.

The New River, brought to London by Sir Hugh Myddelton, was the first pure water supply to the Metropolis. This channel was originally some 40 miles in length, with a total fall of only 16 feet, and conveyed water from the famous Chadwell Spring to the New River Head at Clerkenwell, where the offices of the Metropolitan Water Board now stand. This great work was completed on Michaelmas Day, 1613, when a great pageant was held and speeches made in praise of James I, who guaranteed half the cost. The other half was subscribed by Sir Hugh's friends, called "The Thirty-six Adventurers."

During the recent drought this chalk spring remained dry, except for three days in 1933. On December 1, 1934, water stood at 10 feet below ground level, on December 2 the water level started to rise, and the flow commenced on December 18, and at the end of December the spring was delivering one million gallons, which increased to two by January 2. This shows the rapid response that such springs make to rainfall. The present condition of this originally pure source is a matter of interest, since it has been proved that there is direct communication between it and swallow holes near North Mimms, and within three days fluorescin deposited in the Mimms Hall brook, some 10 miles distant, appeared in the spring. The coli index of this spring has also fallen to $0 \cdot 1$ c.c. Recent tests on the Catherine Bourne at South Mimms have proved a connexion with the Amwell Marsh and Hoddesdon wells, some 12 miles distant, which took six days to show up. It is also practically certain that if the water level in the chalk stood higher than at present, coloration would also appear at Chadwell Spring, showing that a considerable degree of inter-communication occurs within the chalk.

Another well of interest is that of Merton Abbey, depth 332 feet, driven and completed by Dowcra in 1902, for the Southwark and Vauxhall Water Company. During the boring a sudden inrush of water into the shaft held up the work of construction. This well, with a yield of one million gallons, has never been taken into use until this year, when it was used as one of the supplementary sources of supply. Throughout this period chlorination had to be resorted to, since it gave an enormous colony count and showed a variable coli index of 1 c.c. Faulting in the chalk is known to exist in the Merton district.

Between 1878 and 1890, Mr. Bryan, Chief Engineer of the East London Water Company, showed that a rise in the water level in the chalk could be brought about by running filtered water down No. 1 Well at the Lee Bridge Works during the winter time, but of late years this practice has been discontinued, since it was not an economical proposition. The suggested substitution of River Lee water was not adopted, owing to the risk of polluting the chalk.

At the present time there is a considerable discussion in certain localities centring around the disposal of drainage and the need for augmenting the underground supplies. Proposals are in hand to dispose of rainwater and, at the same time, attempt to check the fall in the subsoil water by running surface water into soakaways. As a preliminary, in certain places, fluorescin has been put down, and the excavated area flooded continuously, but up to date no evidence of communication with the Board's wells has been established. Recently an appeal for laboratory assistance was addressed to the Metropolitan Water Board by an

important city in which typhoid cases were occurring, and *B. typhosus* was isolated from 0·05 c.c. of storm water.

From the foregoing, it is evident that the employment of the above procedure must be most cautiously applied and that the vigilance on local supplies must be unrelaxed.

To continue the discussion on wells : About twenty years ago, when the Punjab was being swept with cholera and other epidemics, routine bacteriological examination of wells revealed the presence of coliform organisms occasionally even in greater dilutions than 0·1 c.c. True, the majority of these were not typical *B. coli*, but their presence was disturbing, and innumerable tests only resulted in the exhaustion of the rather valuable laboratory stocks of sugars, &c. Tests on irrigation tube wells showed that although no special care had been taken in their construction they usually supplied a water of high bacteriological purity. It ultimately became necessary to condemn the water supply of Lahore cantonment, and after much discussion the late Colonel Eyre Houston, R.E., installed an experimental tube well at my request.

At first, difficulties were experienced with sand, and in making watertight seals, but when these were overcome the well delivered a water of high purity. Those of you who were acquainted with the records of this cantonment under the old name of Mian Meer will appreciate what a change has taken place in regard to health statistics. In fact, it can be claimed that from that date the character of incidence of water-borne disease completely changed, and the tube has become a common source of supply in Indian towns and cantonments. It is to this type of well that particular attention should be directed, and it undoubtedly merits a greatly extended use. The cost of installation is a fraction of that of a deep well, and it may prove more advantageous to install two or more in preference to laying extensive mains. The linking of two or more wells, in a ring system advocated by Mr. Worger, is an inexpensive method of augmenting supply to more distant areas.

The depth to which such wells can be driven is enormous. A well at Putnam Height, Windham County, Connecticut, has a depth of 6,004 feet. At Louisville, Kentucky, a 3-inch bore carried to a depth of 2,086 feet yields 264 gallons per minute, and its fountain rises 170 feet high. In trial bores at Ambala in India, a depth of 1,000 feet was reached, but without useful results. A recent bore at Swindon yields 2,000,000 gallons a day at ground level.

In the Southern Command, Salisbury area, a considerable fall occurred in the water-level in the chalk during the recent drought. The village of Imber was completely deprived of water by the drying up of the wells, with the exception of a private bore which continued to function. In this locality bores in the greensand gave their normal yield, except that the range of pumping hours had to be increased.

In particular areas the difficulty of the problem is intensified by special conditions, i.e. the relative inaccessibility of water, or a complication such as the high saline content of local supplies, and such places demand a consideration which is disproportionate to their population and importance. In certain villages the development of the well, or water supply, to the local mansion, which is fast disappearing, may yield a sufficiency for standpipes to groups of cottages. In this connexion a reference is invited to a "Water Survey of Essex," written by that eminent authority, Dr. Thresh, some twenty-nine years ago, in which the following significant paragraph appears :—

" Paradoxical as it may appear, Essex, whilst abounding in water, has some difficulty in securing an adequate supply. This is due chiefly to the fact that no well, whether shallow or deep, sunk in any part of the county save the north-west corner, yields a very large quantity, and such springs as occur yield only comparatively limited amounts. But whilst there is this great difficulty in obtaining supplies for the towns and dense centres of population, there is over a large area very little difficulty in obtaining sufficient to supply single houses

and groups of houses, and with suitable arrangements the water can be depended upon as being perfectly wholesome in character."

Those of us who have been brought up in the country are familiar with rainwater as a source of supply, and many have stressed the advantages of, and the economies that would accrue from a more general use of it. In many places it is still the sole supply of villages and mansions, but in certain instances its use is supplemented by that of a subsidiary brackish well for domestic purposes. Though, as a general rule, dual systems are not to be recommended, they are practical propositions, since places like Gibraltar, Bermuda, and Aden are largely dependent upon rainwater. It is stated that the adaptation of the crater at Aden goes back to the time of Alexander, and that the rock faces at Aden and Gibraltar function as dew-ponds condensing appreciable quantities of water.

In the case of small houses, storage of 1,000 gallons capacity has been recommended, but experience rather suggests an increase of this to 2,000 gallons for the ordinary family. Larger houses find it advantageous to supplement this with an additional storage tank, either under the roof, or even at tap level in the lower rooms. Such subsidiary tanks are filled by a pump. Owing to risks of frost, the main storage tank is usually partially below ground level, and this necessitates safeguarding against extraneous pollution. In this country when inadequately protected, they provide a frequent breeding place of the common gnat, *C. pipiens* and also of *Theobaldia annulata*, and the serious epidemic of malarial fever in Jerusalem was related to anopheline infestation of this supply. In other parts of the world the incursions of the vectors of yellow fever necessitate special precautionary measures.

Definite risks also arise from the presence of rats and possible cesspit seepage, and such tanks are therefore constructed on similar lines to wells, being provided with a fixed impervious cover, a coping and the interior rendered in cement. A pump should be fitted, and abstraction by dipper should not be practised. Since roofs are subjected to pollution by birds, fallen leaves, and dust, the fitting of a rainwater separator, which automatically rejects the first washings, is of decided value. The attachment of a roughing sand strainer to the downpipe in conjunction with a simple sand filter in a separate compartment of the tank, are additions which go far to protect the supply, and when all things fail, the inter-position of a flannel, or stockinet bag-strainer is worth consideration. Facilities for cleaning are requisite.

Storage tanks fitted and cared for on the lines indicated have been found to yield a reasonable water at all times of the year, and a little hardening results from the action of water on the cement lining.

Individual household supplies may be supplemented by rainwater installations applied to the church, schoolroom, or groups of barns, but any extensions beyond this bring them in range of separate systems involving heavy costs of pipes and mains, and difficulties regarding control and purification.

The building of special catchment plinths has been claimed to be a most economical method of providing additional supplies, and the suggested employment of dew-ponds is not without its supporters. In the latter case, in many places during the recent drought there appeared to be an absence of the normal S.W. wind, and the prevalence of drying winds may have been a contributory factor in the failure of the dew-ponds.

When surveying waterless areas, apart from communities located on hills, two sets of conditions appear to require differentiation. Either the superficial water supplies, owing to a high saline content, may be unfit for use, or the water-bearing strata may be at a considerable depth. In the first case, the presence of isolated wells or outcrops of relatively sweet water is known to occur even in such areas, and these lend themselves to development; in the latter instance, advantage may be taken of special sand beds, such as the Thanet sands, from which a softer type

of water may be derived. If both of these schemes offer meagre results, the situation can only be dealt with by the importation of water from outside sources, with greatly added costs.

General experience seems to indicate that much could be done by inexpensive tube well systems and bores dotted about an area, which may, in many instances, be linked up with one another, thus augmenting the water supply at more distant places.

The last point to be dealt with is that of water purification and chemical treatment.

Generally speaking, all methods suitable for the treatment of large undertakings are now adaptable to smaller installations. Measures such as filtration, deferization, softening, chlorination and ozonization may be applied mechanically, and the costs of special supervision eliminated.

With river waters and others prone to taste and colour defects, ozone, as a taste remover and the promoter of a fine finish, offers considerable advantages, if the question of costs need not be too closely examined. The more general availability of electricity has also helped in this respect. With this process it is essential that no marked variations in the degree of clarification should occur.

The use of chlorination, followed by filtration through activated carbon, is also strongly supported in certain quarters. For chlorination installations a large variety of gaseous and hypochlorite dosing apparatus presents itself, and the use of electrolytic cells should not be forgotten. All of these may be suitably adjusted for use with ammonia and its compounds, and a greater security attained, particularly with those waters in which adequate clarification cannot be guaranteed.

As regards the smaller supplies, it is felt that methods involving supervision and the careful addition of chemicals will rarely be satisfactorily carried out, and as a general rule it may be wise to restrict advice to simple boiling. Still, it should be appreciated that standardized methods of dosing of buckets and containers of water can be as easily carried out by the uninitiated as the mixing of a seidlitz powder. For conditions in which chemical disinfection can be practised, various hypochlorites in conjunction with hyposulphite, or ammonia and its compounds, can be adapted to "rule of thumb" methods, and even people of the coolie class have proved themselves equal to this control. As a refinement, a sparklet chlorine-generator with ammonia-carbonate tablets provides a very useful combination.

Many people maintain a wholesome rainwater supply, without the use of filters, by the simple expedient of using a flannel-bag strainer and the haphazard addition of a piece of lime to the tank, but an addition of $\frac{1}{2}$ to 1 lb. of lime per 1,000 gallon tank would suffice to disinfect and provide a welcome increase of hardness. In cases where river, or rainwater, tends to have a mawkish taste, a useful improvised taste remover may be made by syphoning water out of a bucket containing a layer of gravel, upon which layers of sand and activated carbon granules and sand are superimposed.

The general conclusions that may be drawn from the foregoing can be summarized as follows :—

(1) There is no golden rule which governs the development of rural water supplies, and each one constitutes a special problem which must be judged on its own merits.

(2) Large and costly schemes involving the laying of long lengths of mains should only come under review when all possible local resources have been fully exploited.

(3) The present trend of developments indicates that in future a very careful watch should be kept upon all conditions which may lead to pollution, or deprivation, of water in all situations. This suggests the necessity for a strong representation of chemical and medical opinion upon all committees that may be set up.

I think that this paper will not have entirely failed in its aim, if it has impressed upon the members of this Section the fact that the problem of rural water supplies is not a parochial matter solely concerned with the supply of water to a few houses and villages, but is a national question of great importance.

Mr. R. G. Hetherington (*Ministry of Health*): In dealing with the problems of rural water supplies I have approached them from the standpoint of an engineer concerned with the design of such schemes and the administrative considerations which are involved in their formulation and execution in this country. I shall therefore deal with what appear to me to be the more important points involved from this standpoint and concern myself entirely with this country.

When we speak of rural water supplies, probably each of us thinks of some little rural village which he knows well and of its water-supply which he probably considers a model either of what a rural water should be or, quite possibly, of what it should not be. When, however, we come to look into the facts it is found that, apply the definition of "rural" as strictly as you like, you still have within the definition water supplies which range from an undertaking covering half a county or more with some hundreds of miles of mains and other works in proportion, down to an old barrel standing outside a cottage door and receiving the water collected from the roof, together, only too often, with a large collection of other things of a less desirable nature.

Now because I have put the large undertaking covering half a county at one end of the scale I do not wish to be taken as implying that I consider such a scheme as of necessity good, or even desirable, in the majority of districts in this country. There are areas in which such schemes are the best and others in which they are the only ones possible, other than the direct collection of rain water—such areas, for instance, as some of the eastern fen-lands where natural sources do not exist of adequate quantity or quality for use as a public supply.

There are two main reasons which make a widespread system of supply undesirable in a thinly populated district of small villages and hamlets—the first is waste and the second is finance. The waste to which I refer is the waste of natural resources—there are all over the country small sources of supply quite adequate for the supply of a village or hamlet and if these are neglected and large distribution systems installed, it means discarding and wasting these small sources of supply, a waste for which the country might well suffer in the future. As to finance, you may accept the proposition that the cost of a water-supply system is concentrated in the mains; once the mains are paid for, the other works necessary—reservoirs, wells, pumping stations, &c.—may be considered a small percentage addition. This overwhelming cost of distribution makes long sterile lengths of main—that is mains from which no supply is drawn and therefore financially sterile—a very heavy dead-weight charge on the undertaking, with the inevitable result of driving up the cost of the scheme. Of course a large, widespread undertaking is bound, in a sparsely populated rural area, to contain long lengths of sterile mains. I have in mind as an example a scheme now in hand which is to supply a whole rural district. This scheme, by no means over-mained, contains 150 miles of mains and if you put the average price of a small main at something between £600 and £700 a mile, you will see the desirability of using local sources where available and avoiding unnecessary lengths of main.

I do not propose to discuss the large widespread rural water undertaking. There is little, if anything, to distinguish it from a similar-sized urban undertaking except the size of the income obtainable in relation to the capital cost.

It is, of course, this question of finance which forms the real difficulty in cases of rural water-supply. An urban scheme supplying a concentrated population and a high rateable value is a paying proposition, that is to say, it can be made self-

supporting on a reasonable water charge. This is not, in general, true of a rural supply, and, assuming that a water rent of 12½% on rateable value is charged—and this is not an undue charge when calculated on low rural assessments—there may be a rate-in-aid, chargeable on the parish as a whole, of a very considerable amount, reaching in a few cases to as much as 4/- or 5/- in the £ and even more. Until comparatively recently this rate-in-aid had to be charged on the parish and there was no alternative, but by recent legislation it is now possible for the Rural District Council to contribute out of the general fund raised on the Rural District as a whole, towards the parish charge and this contribution may be of any size up to 100%; thus by this means a Rural District Council may now make water schemes a general charge on the Rural District. Further there is now a power given to County Councils to contribute out of County funds to such schemes and, in addition, the Government last year placed a sum of one million pounds at disposal to help areas in financial difficulties. In connexion with this sum of one million pounds it may be of interest to note that up to the present time grants have been provisionally allocated to assist schemes submitted by 162 Rural District Councils for 984 parishes; these schemes are estimated to cost, in all, £2,754,355. Thus it is seen that a great deal has been done in recent years to facilitate financially the provision of rural water supply schemes.

Although much has been done to facilitate the provision of rural water schemes there is still often displayed a strong local opposition to a scheme. There is only too often a violent dislike to pay even a moderate price for a good water supply. If a charge of 12¼% on rateable value is made—this is a common standard—it means three-pence a week in the case of a cottage assessed at £5 a year. In such a case a family of say five persons gets an unlimited supply of good water for a week for the price of half a pint of beer and yet this is often argued to be an intolerable burden. Even when it is admitted, and urged in time of a drought, that a scheme is badly needed, a few showers of rain will sometimes reverse the whole local opinion. Not long ago I came across a case in which the water supply to a collection of cottages failed, owing to their wells drying and as a result of this failure and the outcry which accompanied it, a water-main was laid from an adjoining water company's undertaking. By the time the main was laid—and it was carried out very quickly—there had been a few showers of rain and there was a little water in the wells; as a result every cottage refused to take the main supply. Another example, which I cannot help quoting, is of a village which was very short of water and for which a scheme was proposed. When it came to adopting the scheme the large farmer of the district used his influence against it and got it rejected and his argument was this: " In times of drought in this area my grandfather carted water and my father carted water and thank God, I can cart water, so we will not have a piped supply."

So much for the more general aspects of rural water supplies, and although much more could be said I will now turn to a more detailed consideration of the most usual form of a small rural supply. As I have already indicated, it is usual in this country to be able to find a local source which is adequate to afford the supply required by a rural village. Of course in considering a supply, the first factor you have to take into calculation is the amount of water needed per head of population. It is often assumed that this is a fixed figure and that it is merely a question of turning up the reference in a textbook to find what is the demand per head. It is not, however, quite so simple as that, because there are many factors to be taken into account, the most important of which is improved facilities for using water and changes in the habits of the people. If you provide water-closets and baths in all modern houses this is of course going to mean a steadily increasing demand, as new houses are built and old ones modernized. If the larger houses are to have a water supply laid-on to every bedroom this also means an increased demand and if this is to become the general custom in large houses, how long will it be before

similar facilities are provided in those of quite moderate size ? Modern facilities for travelling are bringing into the country village urban dwellers who have been used to urban amenities and the joys of living in the country do not, I notice, prevent such people from wanting to retain what might in some quarters be called urban luxuries.

In the old days a country cottage did not use more than say 3 to 5 gallons per head per day and in many cases considerably less, but then there was no water-closet, no bath and, above all, no hot-water system. It is the facility to draw hot water out of a tap instead of having to boil it in a kettle which increases the demand more than anything else. Now it would not be safe, I think, to put this figure—which used to be 3 to 5 gallons—at much less than 15 or even 20 gallons where water is laid into houses although I am admittedly generalizing, and I recognize that there are peculiar circumstances in nearly every case which have to be allowed for. In some cases of course a standpipe supply is sufficient and is all that can reasonably be urged as being necessary. Such a supply at once cuts down the figure per head, because one of the largest factors in the demand is not the facility for the use of water but the facility for waste.

It was interesting to see the effect of appeals for economy in the use of water during the recent drought; it was not uncommon to find the demand reduced 20% and even 30%, in answer to such appeals. It was, however, even more interesting to watch the effect of the announcements that there was no longer any need for curtailment of demand. Such announcements might have been expected to have the effect of putting back the demand to its pre-drought figure, but this was generally not so, and the demand remained appreciably below the original figure. This goes to confirm that there is much avoidable waste owing to lack of interest by consumers. This lack of interest is no doubt due to the fact that water is not paid for by meter in this country, and therefore a wasteful user knows that he is not running up his bill in proportion to his waste. I am not advocating a system by which domestic supplies are charged for by meter, but in the case of external non-domestic use, such as car-washing and garden-watering, I think it would be desirable to base all charges on meter readings.

Once it has been determined what quantity is required for a rural supply, then the most suitable source of supply has to be found. In this country a suitable source can generally be found within reasonable distance either by sinking a well or impounding a spring. It is desirable to avoid if possible using a source which needs treatment—such as a river—not because the purification cannot be efficiently carried out, but because of the cost and, what is more important, the almost inevitable lack of reliability in treatment in very small schemes. A small village supply cannot afford the staff which is essential for really reliable treatment and has to depend upon more or less unskilled labour, together with some supervision by the health officer and the surveyor, but in such cases accidents will happen, the health officer and the surveyor have too many other duties to perform to be able to do more than give general supervision, and this is really not sufficient to prevent the accident which is almost sure to happen sooner or later.

Assuming that the most suitable source is a spring, the first difficulty which is generally met with is to obtain any reliable data as to the yield. Of course, what the engineer would like is a series of gaugings taken regularly over a considerable number of years and, equally of course, this is what is almost invariably unobtainable. Much can, however, be done to estimate the minimum yield, and it is the minimum that matters, if the geology of the area and the surface characteristics are studied. In this way it is generally possible to obtain some idea of the extent of the strata feeding the spring and the area exposed which forms the collecting ground. In the same way, if the supply has to be sought by sinking a well or boring, the probable yield has to be estimated from geological data and afterwards tested by

trial pumping before more has been spent on the scheme as a whole than necessary. In these questions the officers of the Geological Survey are most helpful and always ready to give advice based on their records and knowledge.

When investigating a source for quantity, it is necessary at the same time to ascertain its quality, which involves chemical and bacteriological analysis. I am not going to say anything about analyses in front of this audience, but I should like to venture one warning which seems sometimes to be needed. There is sometimes a tendency to adopt or reject a source on a long-distance blessing or cursing. However thorough and accurate an analysis may be, I suggest that it cannot fairly be used to pass or condemn a supply without local investigation and inspection. As an example of what I mean, it is not at all unusual to get a bad bacterial analysis of a water supply and on inspection of the source to find an obvious contamination which can readily be removed. Again I will, with great trepidation, venture the suggestion that there is a great difference between two contaminations indicated, for instance by *B. coli*, if it can be shown that one is derived from human and the other from animal sources. I put the question—is there any great risk in a water which may contain some slight contamination obtained, for example, from rabbits? In saying this I must not be taken as advocating the use of water which is contaminated in any way, but I do want to urge that a good sound supply should not be condemned and flung on one side on inadequate grounds, because this only means an unnecessarily costly scheme or, more likely, no scheme at all, and the retention of some inadequate and often grossly polluted system of private wells.

Once a source adequate in quantity and quality has been obtained, the lay-out and construction of a small rural scheme does not offer any serious difficulty. In most cases a supply is obtainable which does not need filtration and all that is required is probably a small pumping station and reservoir or overhead tank and a simple system of mains. Of course if filtration or chlorination has to be adopted it means greater elaboration, but there is no great difficulty from the constructional point of view and the simple form of pressure filter will probably suffice ; as I have pointed out before, however, the real difficulty is centred in obtaining adequate and competent attendance on filtration and sterilization plant within the financial limits available.

There is another aspect of rural water-supplies which merits some attention, namely, the overlooking of and protecting existing individual private supplies. These individual supplies commonly take the form of shallow wells—technically, wells drawing from the surface stratum and not from one overlaid by impervious strata. Where there is an overlying impervious stratum the chief danger to be guarded against is the man who punctures the impervious stratum and proceeds to waste his cesspool contents or other foul matter into the lower pervious stratum and so contaminates his neighbours', as well as his own, supply. In the common case of shallow wells much can often be done to keep the supply pure or even to cure existing contamination. It seems very elementary to say that a well and a cesspool or privy should be as far apart as possible, and yet how often is this simple point neglected. One point about the average cottage well which seems to have almost grown into a faith is that it should never be cleaned out or repaired. It is expected to go on from generation to generation untouched. Much could be done to improve water supplies by cleaning out wells, repairing the brickwork of the sides and preventing percolation of contaminated water through the upper parts of the lining. Then again, the local well is often without any curb round the top to prevent dirty water getting in from the surface of the ground. A well should always have a curb at least six inches high round its mouth and, in addition, an impervious paved area round the top, falling away from the well. Wells with a draw-bucket should have a proper raised stone to stand the bucket on when drawn up ; very often the bucket is dumped down into a dirty muddy patch, only to carry any dirt it manages to pick up down into the well next time it is lowered.

Too little attention is given to the possibilities of collecting and storing rain-water. A well-arranged rainwater supply would often solve many difficulties now encountered in districts which are unfavourably placed for obtaining a well or spring supply. Even in areas that are not unfavourably placed there are often isolated cottages to which it would be a very costly matter to bring water by mains and which would have their conditions greatly improved by a good rainwater system. The great defect which occurs in most rainwater systems is inadequate and unsuitable storage accommodation. The old-fashioned wooden barrel is still I think the most common form of storage and it is not at all a good form. First of all it is very difficult to keep clean and not easy to fit with a proper cover which will keep out dirt and small animals. Next, it is not large enough or, rather, you never find a sufficient number of barrels in use. In areas in which rainwater has had always to be depended upon it is found that a cottage, assuming that it has some auxiliary supply for such purposes as scrubbing, etc. needs 1,000 gallons of storage to see it through a normal summer. This is not a theoretical figure which would in fact be larger, but statistics go to show that a cottage with 1,000 gallons of storage gets through without hardship. With a rainfall of 30 inches per annum a cottage with a roof-area of 500 square feet receives 7,800 gallons of water in a year. If this could all be collected and stored it would be a daily supply of 20 gallons for the household. Although it is impossible to collect every drop of rain, it is possible to collect a very large proportion and there are often outbuildings, etc. whose roofs could also be utilized. Then, again, in a village it is possible to use certain large roof areas such as the church or village hall, etc. to yield a large supply which can be stored for general use, although it should, as a rule, be held for use in prolonged dry periods and not used as a substitute for collection at individual houses. If storage is to be in a very cheap form, some form of galvanized iron water-butt is probably best but it must have a proper lid which can be fixed sufficiently firmly to prevent removal by animals, and, especially, by the small son of the occupier. It should also have a tap above the bottom so that water is drawn from above any sediment in the tank. It is also desirable to have a lower cleaning tap as well, so as to make cleaning-out a simple and easy process. The more easy it is made the more likely is it to be done. The best form of storage tank is one which is constructed underground and from which the water is drawn by a pump. The tank must of course be watertight and this means that good materials and workman-ship must be employed. The interior should be rendered in cement and the walls brought above ground-level for preference. The roof should be rendered outside and there must be a properly sealed manhole of sufficient size to make the process of cleaning out reasonably easy.

Finally, while we shall all agree that improved rural supplies are needed, I would urge that an impossibly high standard should not be aimed at—I have seen so many schemes fail because too high a standard was set and the cost killed the scheme, with the result that nothing was done. If you cannot have a complete piped supply into every house it is a vast improvement, in a village where almost every private well is badly polluted, to have two or three public wells giving pure water, and in many cases a standpipe supply is all that can reasonably be urged as necessary.

Dr. D. W. Boswell (*East Suffolk Rural District Water Supply*) said that many difficulties had to be contended with in East Suffolk. Boulder clay, which was laid down by the glaciers, lay over the major portion of the county except for a small strip along the coast. Water could sometimes be obtained from wells in this area from small deposits of sand or gravel which might happen to lie in this stratum, but as a general rule it must be obtained from ponds. This was possible, as the boulder clay did not allow the water to percolate through. The chalk layer extended underneath through all the county and water could be obtained from it but it was

very deep and compressed, and did not hold much water. In some places the water was red with iron and very unpleasant; also, in parts of High Suffolk the water contained sulphur and was useless, and if ponds were not used here water might have to be carried many miles from chalk-supplies not so affected. Of course there was plenty of water near the broads and rivers in the low-lying areas. In the coastal areas water was obtained from the red crag or gravel pockets.

Wells.—Wells over 30 feet deep, constructed of bricks or concrete rings, were more satisfactory. There was a danger of water collecting behind the bricks from the slug-springs and from surface drainage. This could be prevented by puddling with clay behind the bricks. Shallow wells dried up in the summer and were liable to surface water pollution if too near the sanitary arrangements at the back of the house. Well-covers rotted and rubbish, frogs, mice and snails, etc., got in. A central well on the village green was best, away from the houses. It was constantly working and so was kept purer. Few of the Suffolk wells had dried up during the previous summer.

On analysis the well-water showed :—

1. Chlorine is high. 2·40 parts per 100,000; not more than 3·5 allowed, possibly due to the proximity of the sea :
2. Free ammonia is small if the well is kept working; not over the 0·005 allowed ;
3. Albuminoid ammonia usually high, owing to vegetable matter ; over the 0·01 allowed ;
4. Nitrates high ; over the 0·35 allowed ;
5. Nitrites were found in new wells; these were due to brickwork and sometimes to the greensand.

He, Dr. Boswell, would like to see more mechanical pumps getting water from the chalk, housed in central bath-houses as one saw in Russian villages.

Water-finders.—Professional water-diviners with hazel-twigs were often employed; he did not know if they were genuine or not. He once hid a bottle of water in a garden and the diviner went over the ground and did not find it, but perhaps that was not a fair test. On the other hand, he had seen water found quite easily in Gallipoli, where previously they had been almost dying of thirst, as they had only water which had come from London in petrol tins or was pumped from ships into dirty open boats, which were often upset by half-maddened men and animals. Perhaps if water-finders had arrived earlier, the result of the campaign would have been different, and possibly the end of the war would have come sooner. He would like some scientific information on water-finders.

Ponds.—The disadvantages of ponds were : (1) They might dry up; (2) they might be distant from houses ; (3) it was unpleasant to drink water which had contained frogs, and they might be polluted by tar, if near roads, or by farm animals, etc. Pond-water was certainly soft and was not often subjected to human pollution, and it could be purified by filtration or by boiling.

Rain-water.—Storage was very general, usually to supplement other sources of supply. Round corrugated-iron tanks or tubs were used. There were no artesian wells in his (the speaker's) district, nor was chemical or electrical purification carried out. Boiling was generally advised.

A piped supply from reservoirs was found in about one-third of the houses in the district. The Water Company required 12% to lay pipes on to new houses. This was easily covered by the rates when there were many new buildings together near a main pipe, but the district council was often unwilling to increase the value of isolated private property at the ratepayers' expense, and this caused difficulties. Government subsidies could be obtained.

The Company's water was easily best, but sometimes in the summer it was unsatisfactory. Certain water-plants seemed to flower and taint the water, and when water-weeds were cut bleeding occurred and this had the same effect. Again,

in houses highly situated at the end of the supply the water contained a gross sediment, especially in periods of drought. This was so bad that house-filters became choked at once. It was owing to rust in the upper parts of the pipes, when air had got in through lack of pressure, and possibly was also due to warm, peaty, acid water acting on old iron pipes. Frequent flushing would prevent this, but was often difficult in periods of drought. The new drain-pipes were specially lined to obviate rust. The Water Company would not admit a loss of pressure and said that, on analysis, this water was otherwise fit for domestic use.

He did not remember any recent epidemic caused by East Anglian water, but before 1912 there were epidemics of typhoid due to privy middens leaking into wells. These had been replaced by pail closets, and now they only saw a few odd cases of paratyphoid.

Visitors did not always like the Suffolk water, although the natives throve on it, but then East Anglians sometimes could not drink London water. Vesical stones used to be very prevalent in East Anglia when Cadge of Norwich, whom he (the speaker) knew as a boy, first began to remove enormous numbers. They were now comparatively rare.

Dr. F. R. Seymour said he thought it had been too readily taken for granted that the provision of bulk supplies from a distance was impracticable. Mr. Hetherington had shown that the weekly cost of an adequate water-supply to a household was less than that of a pint of beer, but the fact remained that reasonably good beer could be obtained in most English villages whereas reliable water could not, and he (Dr. Seymour) suggested that in the present stage of civilization it was not unreasonable to expect safe water to be available generally. The total amount of water available in England, Wales, and Scotland should be considered as a whole and the possibilities of its distribution by large regional schemes fully investigated.

Individual supplies would doubtless be necessary in remote places, but at what point should the local needs be considered large enough to justify a bulk scheme ? He was acquainted with a foreign town of 600,000 persons deriving their water from 10,000 local wells. For his own part he suggested that large scale regional planning had been too readily assumed to be outside the range of practical policy, and he was not satisfied that the cost of such schemes would in the long view be prohibitive. He submitted that the capital and maintenance-costs of existing and possible future local supplies might be found to be greater in the aggregate than that of large-scale undertakings.

Dr. H. T. Calvert (*Director of Water Pollution Research, Department of Scientific and Industrial Research*) said that he would like to emphasize another point of view than that which Colonel Harold had expressed, in regard to the discharge of sewage into streams serving as sources of supply. Colonel Harold had said that, in his opinion, a river was better able to exercise its self-purifying properties when it received discharges of effluent in a number of small doses, and whilst this was quite true so long as the discharges were satisfactory in character there was always the danger, at a small sewage-works, of some mismanagement and it seemed to him preferable to have one large works where it would be possible to pay for efficient supervision, than to have a number of small works with the multiplied opportunities for the discharge of inefficiently purified sewage.

There was an increasing tendency to use rivers, which some years ago would have been regarded as totally unsuitable on account of pollution, as sources of water supply and the question arose as to how far a river could be polluted before its use as a source should be condemned. Scientific research by the United States Public Health Service into this question had indicated that the degree of pollution

was higher than might have been expected. He (the speaker) was sure that so long as the country had at its disposal such experts as Colonel Harold, there was little fear that problems of water-purification would remain unsolved.

Mr. D. F. Worger said he was sorry that, though Colonel Harold's paper had referred mainly to rural areas, a large portion of the discussion had reference to urban supplies. As he had entered one of the old companies fifty-seven years ago, and was with them and the Metropolitan Water Board for about forty years, in the last 12 of which he had charge of the supply to South London with a population of two million people, he had had experience of such supplies, but when he retired seventeen years ago, for reasons of health he had to go into a rural district near Princes Risborough and then ascertained the dreadful conditions of districts without a piped water supply ; these included six million people in England and Wales.

About nine years since he was asked to join in a small company to supply Princes Risborough and the adjoining district of some four or five thousand people. Finding that finance was the great difficulty raised by the Ministry of Health and having just heard of a new system, the " Bruston " auto-pneumatic direct pumping into mains without laying a long length of maximum size mains to a reservoir at the highest point, perhaps some miles off, he investigated it, and finally adopted it for the first public installation in the world ; and it had been working since without a single failure. He had since worked out the costs of both systems for 73 places in 22 counties, 51 of which he had visited, and found that in every case there had been a relative financial saving in capital expenditure of between 25% and 45% and in running labour charges of 66%.

The Duke of Richmond's Commission of 1866 strongly formulated the direction that " local water sources be conserved for local consumption " and it was now therefore economically possible to do this for every small source down to less than 1,000 gallons per hour, and the whole difficulty of an economic supply to a small group of houses, or even a large farm or estate, could be entirely overcome. This statement was based on facts, and could not be disputed.

Mr. Hetherington's paper read at the Public Health Congress was a clear, concise and common-sense statement, and together with the contributions to the present discussion, confirmed the fact that decentralization was the solution of rural water-supply difficulties.

Section for the Study of Disease in Children

President—R. C. JEWESBURY, D.M.

[February 22, 1935]

FURTHER REPORTS OF CASES PREVIOUSLY SHOWN

Juvenile Tabes Dorsalis.—C. WORSTER-DROUGHT, M.D.

K. B., now aged 21, shown before the Section in 1924 at the age of 10 (*Proceedings*, 1924, xvii, 18).

In 1923 the physical signs were as follows: Pupils: Right slightly larger than left, Argyll Robertson in type ; knee- and ankle-jerks absent ; some degree of tendo-Achillis analgesia. No Rombergism and no incoördination of upper limbs. Other systems normal. Blood : Wassermann reaction positive. Cerebrospinal fluid : 52 lymphocytes per c.mm., total protein 0·02% ; Wassermann reaction positive ; Lange 0344000000. Mentally the child was quite intelligent, although somewhat emotional. At school she did very well.

Subsequent progress.—From December, 1923 until the end of 1925 she was treated with courses of sulfarsenol (0·3 g.) and bismuth cream (0·4 g.)—four courses during the two years consisting of twelve injections of each substance. Since that time she has been quite well, at work consistently as a shop-girl and suffering only from occasional indigestion.

Present condition.—No symptoms beyond very occasional pains in the legs. She is 5 ft. 5 in. in height and weighs 8 st. 7 lb. The physical signs are as before— Argyll Robertson pupils, absent knee- and ankle-jerks and deep analgesia—-with the exception that she is slightly unsteady in the Romberg position.

Commentary.—This case is brought forward after eleven years to illustrate the relatively favourable prognosis in juvenile tabes dorsalis.

Dr. WORSTER-DROUGHT said that he had not seen this case for seven years until a few days ago ; consequently a further Wassermann test had not been carried out. He would expect, however, to find the reaction positive in both the blood and the cerebrospinal fluid ; it was seldom, if ever, that it became negative in juvenile tabes, in spite of energetic treatment.

He was doubtful if the absence of deterioration could be ascribed to the treatment given during the two years 1924-26. He had been fortunate in being able to observe several cases of juvenile tabes over periods of some years, and in most of them the disease showed little tendency to advance, in spite of the absence of specific treatment. At the same time it was his usual practice to treat these cases by giving two courses a year of acetylarsan and bismuth injections.

Hepatomegaly with Persistent Ketonuria.—C. WORSTER-DROUGHT, M.D.

This patient, now aged 25 years, was shown before the Section twelve years ago (*Proceedings*, 1923, xvi, Sect. Dis. in Child., pp. 56, 60), with the following physical signs : Enlarged liver, the edge being about three inches below the costal margin, firm but not irregular ; spleen impalpable. Urine : sp. gr. 1022, acid, no albumin ; no sugar but acetone and diacetic acid both present. Wassermann reaction negative. Other systems normal.

Several forms of hepatic efficiency tests were carried out with negative results.

It was suggested that the condition was one of constitutional metabolic defect in which the liver was mainly involved.

MAY—CHILD. 1

History.—Birth normal ; breast-fed and perfectly well until a year old.   From the ages of 1 and 4 years she suffered from occasional epileptiform attacks, and between the ages of 3 and 5 from recurrent attacks of vomiting.   During this latter period she did not appear to grow and a medical man said that the liver was enlarged.

Family history.—Father and mother both alive and well, but the mother has otosclerosis.   Both parents showed negative Wassermann blood reactions.   Another child had died twelve years previously at the age of 3 years and he was said by the doctor who attended him to have had an enlarged liver.   A sister three years younger has otosclerosis but normal liver.

Progress.—It has been possible to observe this patient at intervals since 1920— i.e. over a period of fifteen years.   After the demonstration before the Section she remained for several years in much the same condition, the acetone breath and acetonuria being almost invariably present.   In 1925 the liver seemed a little smaller.   In 1930 the fasting blood-sugar was 0·075% and the blood-sugar curve showed a delayed fall.   The patient showed a certain degree of infantilism.   In 1932 she was bodily and mentally well developed, although puberty had been delayed until the age of 17.   The liver was no longer enlarged ; nevertheless her breath usually smelt of acetone and she continued to show a slight acetonuria but no diacetic acid.   Glycosuria has never been detected, and the blood-count was invariably normal.

Present condition.—The patient is now free from all symptoms but occasionally shows an acetone breath.   There is still a trace of acetone in the urine (January 1935) but no diacetic acid.   Her height is 5 ft. 6½ in. and weight 9 st. 8 lb.   The liver is not enlarged.

Commentary.—The case is shown to illustrate the excellent prognosis in this condition as the patient seems to have practically " grown out " of her disease, which was clearly of constitutional metabolic origin.   The exact nature of the metabolic defect in question was not apparent until E. von Gierke in 1929 made a post-mortem examination of a girl aged nearly 8, who had died from influenza and was known to have had persistent enlargement of the liver of unknown origin.   He found that the enlargement of the liver was due to excessive accumulation of glycogen.   In an elaborate article he described the condition under the heading " Hepato-nephro-megalis glykogenica—Glykogenspeicherkrankheit der Leber und Nieren."

A similar glycogen accumulation was found in the liver of a boy aged 4 years and 10 months who died of pneumonia.   In the liver of the former patient, Schonheimer, who undertook the chemical examination, found absence of the glycogen-splitting ferment which can be detected in normal livers.   It seemed, therefore, that the enlargement of the liver was due to defective transformation of glycogen into sugar and to the resulting accumulation (storing) of glycogen in the hepatic parenchyma.   The girl's kidneys also showed some accumulation of glycogen.

During life the presence of glycogenic hepatomegaly can only be proved definitely by the microscopical examination of an excised piece of the liver or of material obtained by liver puncture.   Without this procedure, however, it should be possible to arrive at a diagnosis of the disease, minor forms of which are perhaps not so extremely rare.   The most important feature of the disease is an enormous enlargement of the liver, without splenomegaly, and present from early life.   The second feature to be noted is the presence of hypoglycæmia without the usual clinical signs of the condition, while a third is the fact that according to Schall the glycogen cannot be mobilized by an injection of adrenaline.   Ketonuria, obesity, infantilism and a certain weakness of the skeletal musculature may also be present.

A clinical diagnosis is justified in the following circumstances : A child has considerable uniform enlargement of the liver which feels smooth and not especially hard or tender. The patient does not appear really ill, has never been jaundiced and shows no enlargement of spleen or lymphatic glands. The urine may be found to contain ketones week after week and even year after year. Apart from starvation, persistent vomiting, or a special ketogenic diet, there is no disease in which such chronic ketonuria, without glycosuria, is possible. In some cases the ketonuria is slight or absent. Finally, there is the presence of hypoglycæmia and the effect of adrenaline on the blood-sugar to be taken into consideration.

This case appears to have been the first record of the condition and no further contribution to the disease appeared until von Gierke's papers of 1929 and 1931. Subsequent cases have been reported in Germany by L. Schall (1932), O. Muck and E. Unshelm (1934); in England by E. Bellingham Smith and E. O'Flynn (1933), E. C. Warner (1933), R. W. B. Ellis (1934), and P. Watson (1934); in Australia by H. J. Solomon and P. M. Anderson, A. H. A. Court and S. D. Bray (1934) and in Holland by S. van Creveld (1934).

Dr. F. PARKES WEBER said that a main point of interest in regard to this case, and also in regard to that shown by Dr. R. W. B. Ellis, was the obvious tendency to "grow out" of an "inborn metabolic error," which was apparently the same as that in which von Gierke had shown the enlargement of the liver to be due to the accumulation of glycogen in the hepatic cells.

Acute Hæmoglobinuria and Anæmia in a Boy.—F. PARKES WEBER, M.D.

The patient, R. V., aged 6 years, was shown three years ago, as a remarkable case of acute hæmoglobinuria and anæmia, with rapid recovery following a single blood-transfusion (*Proc. Roy. Soc. Med.*, 1932, xxv, 715). At the meeting I suggested that the case represented the acutest form of Max Lederer's "acute hæmolytic anæmia" (*Amer. Journ. Med. Sci.*, 1930, clxxix, 228), and that the case of a boy, aged 11 years, whom I showed at the Clinical Section on October 9, 1931 (*Proc. Roy. Soc. Med.*, 1932, xxv, 15), was a more characteristic example of Lederer's anæmia, without hæmoglobinuria. There was hæmoglobinuria in some of the cases referred to by Lederer.

In neither of my patients has there been any recurrence, though the latter one has suffered from an attack of catarrhal jaundice since I showed him.

Dr. N. B. CAPON said that in a case of acute anæmia in a baby, aged 6 months, at present under his care, the chief features were rapid onset of anæmia, with marked splenomegaly, absence of jaundice, slight diminution of red-cell resistance, and weakly positive indirect van den Bergh reaction. The infant was breast-fed and there was no evidence of rickets. The treatment at present consisted of repeated blood-transfusions.

Actinomycosis of Lung.—T. S. RODGERS, M.D. (by permission of A. G. MAITLAND-JONES, M.D.).

This case was shown at a meeting of the Section in January 1933, by Dr. R. W. B. Ellis, by permission of Dr. Maitland-Jones. (For previous report see *Proceedings*, 1933, xxvi, 513, Sect. Dis. in Child., 33.)

N. P., a boy, now aged 7 years and 11 months.

Progress.—Intensive iodide therapy was started as soon as the diagnosis was made, the dosage being increased up to 120 gr. a day for several weeks. The boy has had from 40 to 60 gr. a day almost continuously during the past two years, except for one three-month period during which it was remitted.

The temperature and respiration rate fell to normal on the third day in hospital, and except for one or two slight rises (to 101°), the boy has been afebrile since

that time. The chest wound continued to drain small quantities of sero-sanguineous discharge and thin pus for six to eight weeks, and then healed. A second small fluctuant swelling appeared on the chest-wall, posterior to the old wound, five months later, but settled without incision.

The general health has improved slowly during the past two years, and the boy has gained 8 lb. in weight. Apart from slight dyspnœa on exertion he is free from symptoms. The physical signs in the chest remained practically unchanged for nearly twelve months, although a skiagram showed some degree of clearing. Since that time there has been considerable improvement in both radiological and physical signs. There is now (February 1935) an impaired percussion-note over the right lower lobe only, and slightly diminished air-entry in this area. The clubbing of the fingers is definitely less marked.

Radiological examination (7.2.35) shows marked clearing of the right lower lobe, with some residual fibrosis at the base, pleural thickening and slight displacement of the heart and trachea to the right.

Hyperthyroidism dating from Infancy.—R. W. B. ELLIS, M.D. (by permission of Dr. DONALD PATERSON).

G. W., a girl, aged 14 years. There is no family history of goitre or exophthalmos. The mother was in good health and was aged 31 when the child was born. A brother aged 12½ is normal. Since earliest infancy (? since birth) the child has had well-

Hyperthyroidism, dating from infancy.

marked exophthalmos, which is clearly seen in a photograph taken at the age of 4½ months. Throughout childhood she has been very " nervous " and has had a fine tremor. She attended the Hospital for Sick Children, Great Ormond Street, as an out-patient under Dr. Paterson at the age of 10 years, and was shown before

this Section at that time.[1] She then had fullness of the thyroid and tachycardia. At the age of 8 she had a fit at school, and has had frequent "vacant turns," of petit mal type, since then. She has been treated with arsenic and bromides, and with tincture of iodine. During the past eighteen months, she has become considerably quieter and the exophthalmos less marked. For the past fifteen months she has menstruated irregularly. She complains of pains in the abdomen and recurrent headaches, and gets easily tired in hot weather.

On examination.—A well-developed girl of 14, who has reached puberty. There is fullness of the thyroid, a fine tremor of the outstretched hands, and a relatively slight degree of exophthalmos. Von Graefe's and Stellwag's signs present. Pulse-rate 106, with occasional extra-systoles.

Comment.—The principal interest of this case lies in the early age at which the first symptoms became manifest, and the duration of the disease throughout the whole period of childhood. Exophthalmos was certainly present at the age of four months (see photograph published with previous report), and possibly from birth. The number of recorded examples of exophthalmic goitre dating from early infancy is still extremely small. Mr. Clifford White has kindly called my attention to a case which he reported before the Section of Obstetrics in 1911 [1]; an infant, whose mother had developed Graves' disease during pregnancy, was born with typical exophthalmos and a goitre. Histological examination of the thyroid showed the characteristic changes. This case is certainly unique in that the diagnosis was suspected *in utero* from the fœtal heart rate. A somewhat similar case is quoted by Ochsner and Thompson. A premature infant, the fourth child of a mother who had developed Graves' disease during her first pregnancy, and had become worse during each succeeding pregnancy, was found to have exophthalmos at the age of five weeks. In this instance the condition had improved considerably by the age of 27 months. Rowstron recorded exophthalmic goitre in a child of $4\frac{1}{2}$ months, suffering from congenital syphilis, and Elliott has recently reported the case of a child in whom the symptoms dated from six months of age. Subsequent operation was followed by hypothyroidism. Klaus found the condition in an infant of nine months, and Helmholz in one of eleven months of age.

Such cases, in which the condition dates from infancy, are obviously too few for any confident prognosis to be given, and it is an open question as to whether, or when, operation should be attempted. This particular patient has been treated medically, and has reached and passed puberty without the condition interfering seriously with her ordinary life. Her general state appears slightly better, rather than worse, than it did five years ago.

REFERENCES

WHITE, C., *Proc. Roy. Soc. Med.*, 1911-12, v (Sect. Obst., 247).
OCHSNER, A. J., and THOMPSON, R. L., "The Surgery and Pathology of the Thyroid and Para-thyroid Glands," London, 1910, p. 192.
ROWSTRON, N. F., *Brit. Med. Journ.*, 1922 (i), 347.
ELLIOTT, P. C., *Journ. Ped.*, 1935, vi, 204.
HELMHOLZ, M. F., *Journ. Am. Med. Ass.*, 1926, xxxvii, 157.
KLAUS, O., *Prag. med. Wchnschr.*, 1914, xxxix, 515.

Hepatomegaly in an Infant. (? Hepatomegalia Glycogenica ? Hypertrophic Steatosis).—R. W. B. ELLIS, M.D. (by permission of Dr. ROBERT HUTCHISON).

A. H., a girl, aged 19 months, has been in good general health since birth, but was admitted to the Hospital for Sick Children under Dr. Robert Hutchison in October 1933 (aged 3 months) on account of the enormous size of the abdomen,

[1] *Proceedings*, 1930, xxiv, 569 (Dis. in Child., 27).

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which was thought to have been large since birth, but had increased rapidly since the age of 2 months. The child was shown at the meeting of the Section held on October 27, 1933.[1] At this time, the abdomen was distended with the smooth firm mass of the liver, the right lobe of which reached to the pubis, and the left two-fingerbreadths below the umbilicus (fig. 1). The possibility of the condition being due to a neuroblastoma of the adrenal metastasizing in the liver was discussed, and the suggestion was made that the condition was more probably an example of hepatomegalia glycogenica (von Gierke's disease). Subsequent investigations partly confirmed the latter view. The resting blood-sugar tended to be low, but no acetone

FIG. 1.—A. H., aged 4 months.   Liver margin marked above pubes.

was found in the specimens of urine examined. Injection of adrenalin showed a relatively poor blood-sugar response, with a rise of less than 30 mgm.

During the past sixteen months, the child has progressed normally, and the decrease in size of the liver has been very striking. She now weighs 22½ lb., and measures 31 in. She appears to be in excellent health. The right lobe of the

1 *Proceedings*, 1933, xxvii, 118 (Dis. in Child., 6).

liver is palpable as a firm mass in the right loin, and the liver margin extends two-fingerbreadths below the costal margin (fig. 2). The spleen is not palpable.

Comment.—The enormous size of the liver when this infant was shown at the age of four months inclined several members of the Section to regard the condition as malignant. From the child's subsequent progress, the diagnosis now appears to rest between an accumulation of glycogen in the liver (von Gierke's disease) and "stéatose hypertrophique" of the type described by Debré and others. That the

Fɪɢ. 2.—A. H., aged 18 months. Liver two fingerbreadths below costal margin.

latter condition may result in chronic hypoglycæmia and a defective rise of blood-sugar after the injection of adrenalin has recently been shown by Kramer, Grayzel and Solomon, and it will clearly be extremely difficult to distinguish between the two conditions except by biopsy (which clinically has hardly appeared justified), or post-mortem examination (which appears progressively more remote). From the fact that the hepatomegaly dated from early infancy and was unassociated with any symptoms, I was inclined to regard this as an example of von Gierke's disease, though the findings were not by any means conclusive.

<div style="text-align:center">REFERENCES</div>

DEBRÉ, R., and SÉMÉLAIGNE, G. *Presse méd.*, 1930, xxxviii, 1742.
KRAMER, B., GRAYZEL, H. G., and SOLOMON, I. *Journ. Ped.*, 1934, v, 299.

POSTSCRIPT (2.5.35).—Blood glycogen $14 \cdot 1$ mgm.% ; blood cholesterol 170 mgm.%.

Discussion.—Dr. HELEN MACKAY said that she was particularly interested in this case because she had recently seen, at the Queen's Hospital for Children, a baby who on clinical examination was extremely like the present one when first shown by Dr. Ellis. This infant was a boy, aged 5 months, whose abdomen had been noticed to be large from one month of age, or according to another account, from birth. He was thought by his mother to be well, and took his feeds readily. He had "always been pale." His birth-weight was 5 lb. 10 oz. He was breast-fed till 8 weeks old, and was subsequently given ostermilk. There was one sister, aged 13 years, who was reported healthy.

On admission, the baby was fairly well nourished, weighed 14 lb. 14 oz., had a very large abdomen, and a hypochromic anæmia (hæmoglobin 56%, with a few nucleated red cells in the blood-film, and a normal white cell count). The liver occupied most of the right side, and a large part of the left side, of the abdomen—reaching the extreme inferior limit of the right iliac fossa. She thought that, as in Dr. Ellis's case, small irregularities could be felt on the surface of the liver, whereas in the case of glycogen disease reported on by Dr. E. Bellingham Smith and Dr. E. O'Flynn from the Queen's Hospital, the liver had a smooth surface, as shown at post-mortem examination. Dr. O'Flynn had also investigated her (Dr. Mackay's) case. The van den Bergh reaction was negative, direct and indirect ; the urine showed no acetone on repeated examinations, and injection of 1 minim of adrenalin produced a rise of 0·033% in the blood-sugar curve. The blood glycogen was 17 mgm. % (normal 12 to 20 mgm. %). The Wassermann reaction was negative. The child died at home with an enteritis, and no post-mortem examination was made.

Dr. S. van Creveld (who had carried out extensive investigations on several cases of von Gierke's disease) said that on account of the adrenalin blood-sugar response he would be unwilling to diagnose either this case of hepatomegaly, or that recently shown by Dr. Alice King before the Section, as examples of glycogen disease ; nevertheless, the clinical similarity, the long history, with fairly good general health and progress, and the absence of jaundice inclined her (Dr. Mackay) to think that they must be so. The evidence brought forward at this meeting by Dr. Ellis and Dr. Worster-Drought that such striking improvement was possible in von Gierke's disease was of great interest, because it threw an entirely fresh light on this disease. Since recovery was possible, information concerning any changes in the biochemical findings, including the adrenalin response, in the different stages of the disease would be very interesting and would assist in the diagnosis of other cases. It seemed probable that a different adrenalin effect would be produced in different stages of the metabolic defect.

Dr. PARKES WEBER said he thought that many of the old cases of hepatomegaly in infants were really due to extreme fatty infiltration of the liver, and that some of them were possibly due to a metabolic defect—namely, an inability to make use of the fatty droplets accumulated in the liver cells—analogous to the inability to make use of the glycogen accumulated in the liver cells in cases of von Gierke's disease.

Facial Tumour.—R. H. BAILEY, M.B., B.Chir. (for Dr. DONALD PATERSON).

E. O., a girl, aged 11 years and 11 months.

Case shown at a previous meeting of the Section as one of zygomatic tumour with ? papillœdema of both discs (*Proceedings*, 1935, xxviii, 412, Sect. Dis. in Child., 26).

Further report.—No further physical signs developed, and the child was discharged with the diagnosis of "local zygomatic tumour," the condition of the discs having no connexion with the tumour.

3.1.35 : Admitted under Mr. Rock Carling for exploration of tumour.

Small incision made over zygomatic process. When the temporal fascia was incised a cystic swelling appeared in which was a small cavity surrounded by some necrotic tissue. The bone appeared to be normal.

Pathological report (Dr. R. J. V. Pulvertaft).—No evidence of tuberculosis or neoplasm ; suggest chronic inflammation following trauma.

Culture : Sterile.

Specimens from a Case of Congenital Obstruction of the Œsophagus.—
HAZEL CHODAK GREGORY, M.D.

Case reported October 26, 1934, see *Proceedings*, 1934, xxviii, 141 (Sect. Dis. in Child., 1).

Pathological specimens : Stomach and œsophagus : microscopic section.

Subsequent history.—The œsophageal obstruction increased and could not be overcome by the smallest bougies, in fact was definitely worse after the attempt. The child's weight dropped rapidly and it became necessary to perform gastrostomy to prevent starvation. It is worthy of note that within twenty-four hours of opening the stomach the œsophageal passage became clear, and subsequently all fluids were taken easily by mouth and not regurgitated. By this time, however, the patient was very weak and died seven days after operation with a terminal bronchopneumonia.

At autopsy the diaphragm was found to have normal attachments. There was no great deficiency in the diaphragmatic muscle as suggested by the skiagram, but a finger could be passed up easily between the muscle and the œsophagus, and it is evident that the irregular protuberance of the stomach seen in the radiogram was a peristaltic wave. The dome of the diaphragm stood high on either side. The œsophagus was short, so that the cardiac end of the stomach was drawn up into the thorax. There was no obstruction to the passage of a bougie down the œsophagus, and on opening it up there appeared to be no narrowing of the lumen, no obstructing folds, and no stenosis, but only a rather unusual puckering of the stomach where it joined the œsophagus. A shallow ulcer at the extremity of the œsophagus was almost certainly due to instrumentation.

Microscopically, a section of the cardia shows the normal passage of pavement epithelium into gastric mucosa.

Specimens from a Case of Right-sided Hemihypertrophy associated with Pubertas Præcox.—JOAN HARWOOD, L.R.C.P., M.R.C.S., and ELIZABETH O'FLYNN, M.D.

Summary of Previous Report (*Proceedings*, 1932, xxv, 951, Sect. Dis. in Child., 65).

A. C., a boy, aged 6½ years, was brought up to the Queen's Hospital for Children, having had one leg shorter than the other, since birth. Height 4 ft. 3 in., weight 4 st. 9 lb. On examination there was found to be right-sided hemihypertrophy, associated with hyperplasia in both testes and the penis, the right testis being larger than the left. He showed no other sign of secondary sexual development, his habits were normal, and he was an intelligent child. No nævi were present.

Laboratory examinations were all negative ; X-ray examination of the pituitary fossa showed no abnormality, and the epiphyses were normal. Uroselectan X-ray examination of the urinary tract showed a large but normal-looking left renal shadow ; while the right renal shadow was large, with an irregular outline at its upper pole, the appearance being suggestive of a renal tumour on the right side.

Examination under anæsthetic revealed a palpable tumour in the right loin.

Present report.—Operation by Mr. E. A. Crook, F.R.C.S., June, 1932, disclosed a large round encapsulated tumour, about 3½ in. in diameter, situated in the right adrenal region. The capsule of the tumour was very vascular and thin, and the perinephric fat showed great vascularity. The tumour was easily separated from the upper pole of the kidney, and was removed. (Microscopical examination showed an adrenal adenocarcinoma.)

Recovery from the operation was uneventful, and the patient lived a normal life for six months. He was then brought up to hospital on account of a fit, which followed sudden temporary loss of consciousness. On admission he had three

violent epileptiform fits, mainly affecting his limbs and the right side of his face. These fits were followed by marked weakness of the right side of the body, with loss of tendon and abdominal reflexes, and an extensor plantar response on the right side. The left pupil was larger than the right, both reacted to light, and there was slight papillœdema of both discs. He could recognize his parents on regaining consciousness. The following day his speech was thick, and there was nominal aphasia. Four days later there were no abnormal physical signs in the central nervous system, and the aphasia had disappeared. His height was then 4 ft. 3¾ in., his weight 5 st. 4 lb. 10 oz., and there was a large hard palpable mass in the right loin.

A fortnight later, sudden temporary unconsciousness was followed by violent clonic movements, at first right-sided, and then generalized. There were severe muscular spasms of the whole body, and cyanosis was marked. Controlled only by deep surgical anæsthesia with chloroform. The optic discs were engorged, and the right pupil was larger than the left. Tendon reflexes were brisk, there was ankle clonus, and the abdominal reflexes were present. The plantar response was flexor.

Twenty-four hours after recovery of consciousness there was a sudden change; the patient commenced crawling about the bed on all fours, grinning sheepishly and wagging his finger at imaginary objects, and chuckling without reason. He took no notice of anyone, though at first he glanced towards the ward door when it opened, possibly looking for his parents. Later there was verbigeration and negativism, with delayed reaction to painful stimuli. He laughed at any other stimulus. The right pupil was larger than the left, both were a little dilated and both reacted to light; the optic discs were normal. Reflexes were brisk.

Control was difficult; morphia, hyoscine, paraldehyde, bromides, and chloral had no effect. Large doses of luminal produced a little sleep. Three moderately quiet days followed, with intervals in which he recognized his parents; on the fourth day he became maniacal. He was either controlled by drugs or stuporous until he died 10.3.33 (six weeks later). He ate well throughout, but lost weight rapidly.

Report on autopsy thirty-six hours after death.—Boy aged 8½ years, big for his age; marked asymmetry of whole body; the right side being much larger than the left. Hirsuties of lip, pubis and legs. Healed operation-scar in right lumbar region.

Abdomen: A large mass is present in the right loin. It is encapsuled and not adherent to surrounding structures. It overlies and obscures the right kidney. Weight 671 grm. Its cut surface looks partly cystic, partly hæmorrhagic, with a central zone yellowish-brown in colour. No suprarenal tissue recognized in the tumour. Attached to its lower pole are a few soft nodules, whitish and homogenous in appearance. No peritonitis and no deposits within the abdomen.

Kidneys: Right weighs 182 grm.; left weighs 148 grm.; both appear normal but enlarged.

Right suprarenal: Replaced by tumour; left suprarenal: 6·5, looks normal.

Bladder: Healthy. Spleen: 171 grm.; definitely lymphoid. Pancreas: 195 grm.; greatly enlarged, firm and tough. The tail is relatively more hypertrophied than the head. Liver: 1,132 grm. congested. The right lobe looks larger than normal. The upper pole of the tumour is loosely bound to it, but does not invade it. Intestines normal.

Thorax: Pleura, about 3 oz. of blood-stained fluid in left chest; none in right. A few small deposits on both pleura, none larger than a pea, and tending to be raised and pedunculated. On incision they are soft and pale. Lungs: Emphysema and congestion. No deposits. Thymus: 15·25 grm.

Pericardium healthy. Heart: 256 grm.; muscle good; left ventricle hypertrophied.

Skull: No deposits in the skull bones. Brain: Shows slight pressure cone; some œdema; no metastases or other abnormality. Left hemisphere 640 grm.; right, 604 grm.

Genitalia : Penis enlarged.   Both testes enlarged, right more than left.

Histological appearances.—The tumour removed at operation consists of large polygonal cells with darkly staining nuclei arranged more or less in columns.   The resemblance to the zona fasciculata and reticulata is definite.   The tumour removed at autopsy is less typical.   It is much more malignant looking, more necrotic. Many of the cells contain a fuchsinophil material similar to that seen in the cortical cells in cases of virilism.

Kidneys : Contain patches where the tubules are dilated, epithelium flattened and somewhat degenerated.   Lungs : Emphysematous.   The pleural nodule embedded in the lung tissue is identical with the primary growth.   Spleen : Lymphoid. Pancreas : In addition to hypertrophy shows signs of cellular activity, and the islets appear to be more numerous than usual.   Fibrosis and some necrosis in the centre of the lobules.

The right testis shows an attempt at spermatogenic development, as seen in testes at the ages of 13 or 14.   The left testis appears less developed.

Thyroid : Normal, with possibly diminished colloid.

Discussion.—Dr. ELIZABETH O'FLYNN suggested, as an explanation of the occurrence of fits in the absence of metastases, that they might have been of hypoglycæmic origin, consequent upon hyperinsulinæmia.   In support of this view she might mention the great enlargement of the pancreas found at autopsy, and the absence, during life, of any appreciable rise in blood-sugar on the ingestion of glucose.   The curve never reached the 100 mgm. level, with a resting level of 60 mgm.

Dr. PARKES WEBER said that this case was of extreme interest, as illustrating the occurrence of overgrowth of only one half (the right half) of the body (hemi-macrosomia) in response to a growth-promoting hormone, produced by the suprarenal cortical tumour.   In the previous discussion, when the patient was shown, he had referred to what he had written on that interesting question.

Another extremely interesting point was the one mentioned by Dr. O'Flynn, namely, that relative hyperinsulinæmia might have been set up by the operation, resulting in death with hypoglycæmia.

Specimens from Case of Congenital Hyperplasia of the Suprarenal Cortex.—J. VERNON BRAITHWAITE, M.D.

Report of operation and post-mortem examination.

This case was shown at the meeting of the Section held in November 1934, under the title of Giantism, Virilism, and Pseudohermaphroditism (*Proceedings*, 1934, xxviii, 148, Sect. Dis. in Child., 8).

Operation (Mr. Robert S. Lawson) : Adrenalectomy (Left Side).—Under spinal anæsthesia and gas-and-oxygen, with a pre-anæsthetic of paraldehyde, the abdomen was opened by a left paramedian incision.   No gross tumour could be felt in the region of either suprarenal, and the uterus, ovaries, and tubes appeared to be normal and of a size consistent with the age of the patient.   The right ovary was removed for microscopical examination and the left suprarenal gland was then exposed by incising the gastrocolic omentum, retracting the stomach over to the right side and the transverse colon downwards and to the left, and then by dividing the peritoneum just above the tail of the pancreas.   The capsular vein of the suprarenal was exposed, clamped and divided ; by careful dissection the arteries were isolated and ligatured.   After this the gland was removed fairly easily. Unfortunately, during the whole of the operation, in spite of the spinal anæsthesia, the stomach and bowels were in a state of extreme distension which increased the difficulty of the operation and probably produced the shock from which the child died.   A possible explanation of this distension is that the amount of adrenaline present in the blood was able to overcome the effect of the spinal anæsthetic, and so prevent it paralysing the sympathetic nerves supplying the stomach and bowels.

(Systolic blood-pressure 135.) The gland proved to be very much larger than normal and was spread over the whole of the upper pole of the kidney.

Post-mortem report (Dr. W. W. Mackarell).—The whole of the operation wound is clean. No hæmorrhage. Heart: Weight 5½ oz.; some hypertrophy of right side. Brain: Pineal slightly larger than normal (0·3 grm. in weight; normal 0·2 to 0·25 grm.). Pituitary not enlarged. Kidneys: Weight 2½ oz. each; very pale, very little distinction between cortex and medulla, otherwise normal. Lungs: normal. Liver: Weight 21 oz., soft and pale. Thymus: Very large, and there are some petechial hæmorrhages, 44 grm. in weight (weight average at birth 7·7, increased to 15th year when weight averages 20 to 28 grm.); no enlarged lymphatics seen. Spleen: Weight 2½ oz.; normal. Stomach and intestines: Normal. Left ovary: Small and appears normal. Right has been removed.

Right suprarenal: Large (about the size of the left, which has been removed); weight 24 grm.

Microscopical examination.—Suprarenal: Normal suprarenal tissue. Ovary: Normal functioning ovary, except that there are two tiny collections of cells which might possibly be testicular cells, although they are by no means typical. There are two large unerupted graafian follicles, one of which contains a recent hæmorrhage.

Dr. PARKES WEBER said that the case certainly corresponded exactly, with its macrosomia, virilism and pseudohermaphroditism, to those cases in which so-called "inter-renalism" had commenced during intra-uterine life. Perhaps an acute endocrine upset, as a first result of the operation, had had to do with the child's death.

Section of Medicine

President—Sir FARQUHAR BUZZARD, Bart., K.C.V.O., M.D.

[*February* 26, 1935]

The Glands of the Stomach in Relation to Pernicious Anæmia; with Special Reference to the Glands in the Pyloric Region

By E. MEULENGRACHT (Copenhagen)

ABSTRACT.—The researches have had in view the anatomical localization of the anti-anæmic factor (Castle's " intrinsic factor ") in the stomach.

As the pig's stomach is peculiarly constructed, having a so-called cardiac-gland region, a fundus-gland region and a pyloric gland region continued in the glands of Brunner in the duodenum, preparations have been made from each of these regions, and tests of the effectiveness of each of these separate portions have been made in cases of pernicious anæmia. It has previously been pointed out (Meulengracht and Schiødt) that the production of hydrochloric acid, pepsin and rennin was confined to the glands of the fundus region (peptic glands) with their oxyntic cells and chief cells.

The experiments showed that the extract of the fundus-gland portion was inactive in cases of pernicious anæmia, that of the so-called cardiac-gland portion was mildly active, that of the pyloric-gland portion was strongly active, and that of the duodenal portion was also strongly active. The feebler activity of the cardiac portion might be shown to be a result of the smaller number of glands to the unit area in that region.

The conclusion drawn from the experiments is that the so-called cardiac glands, the pyloric glands and the Brunner glands in the duodenum, which anatomically may be said to be very nearly identical, may also be taken to be functionally identical, at any rate with regard to the production of the anti-anæmic factor.

This collective gland region, which it is proposed to call the pyloric-gland region, is the site of the production of the anti-anæmic factor. There is thus attributed to these glands a definite, well-defined and vitally important function.

It is further concluded from the experiments that pernicious anæmia in human beings is due to atrophy and inactivity of that part of the stomach which comprises the pyloric-gland region. The experiments may thus be said to have anatomically localized pernicious anæmia in human beings.

Experimental pernicious anæmia will presumably be producible by the deliberate removal of the pyloric-gland region.

Stomach preparations for the treatment of pernicious anæmia will with advantage be producible from the pyloric-gland region alone.

RÉSUMÉ.—Le but de ces recherches a été la localisation anatomique du facteur anti-anémique (" intrinsic factor " de Castle) dans l'estomac.

Comme l'estomac du porc a une structure spéciale, consistant en trois régions, appelées région des glandes cardiaques, région des glandes fundiques, et région des glandes pyloriques, continuée par la région des glandes de Brunner dans le duodénum, des extraits de chacune de ces régions furent préparés, et leur efficacité dans le traitement de l'anémie pernicieuse fut déterminée. Meulengracht et Schiødt ont déjà montré que la production d'acide chlorhydrique, de pepsine et de présure est limitée aux glandes de la région fundique (glandes peptiques), avec leurs cellules de revêtement et cellules principales.

Les expériences ont montré que l'extrait de la région des glandes fundiques (glandes peptiques) n'a aucun effet dans l'anémie pernicieuse, celui de la région dite des glandes

cardiaques est faiblement actif, celui de la région des glandes pyloriques est fortement actif, et celui du duodénum est aussi fortement actif. L'activité plus faible de la région des glandes cardiaques pourrait s'expliquer par le plus petit nombre de glandes par unité de surface dans cette région.

La conclusion tirée des expériences est que les glandes dites cardiaques, les glandes pyloriques et les glandes de Brunner dans le duodénum, qu'on peut considérer comme presque identiques anatomiquement, peuvent aussi être considérées comme identiques du point de vue fonctionnel, en tout cas en ce qui concerne la production du facteur antianémique.

C'est dans cette région glandulaire collective, qu'on propose d'appeler région des glandes pyloriques, qu'a lieu la production du facteur antianémique. On attribue donc à ces glandes une fonction définie et nécessaire à la vie.

L'auteur conclut, en outre, que l'anémie pernicieuse chez l'homme est due à l'atrophie et à l'inactivité de la partie de l'estomac formant la région des glandes pyloriques. On peut dire que ces expériences ont localisé anatomiquement l'anémie pernicieuse chez l'homme.

Il sera probablement possible de produire l'anémie pernicieuse expérimentale en extirpant la région glandulaire pylorique.

Il sera avantageux d'employer seulement la région des glandes pyloriques pour la préparation d'extraits d'estomac destinés au traitement de l'anémie pernicieuse.

ZUSAMMENFASSUNG.—Gegenstand der Untersuchungen war die anatomische Lokalisierung des antianämischen Faktors (Castle's " intrinsic factor ") im Magen.

Da der Schweinemagen insofern besonders gebaut ist als er in einen Kardiadrüsenabschnitt, Fundusdrüsenabschnitt und Pylorusdrüsenabschnitt zerfällt, welch letzterer in den die Brunnerschen Drüsen enthaltenden Teil des Duodenums übergeht, wurde aus jedem dieser Teile ein Präparat hergestellt und dessen Wirkung bei perniziöser Anämie untersucht. Meulengracht und Schiødt haben schon früher darauf hingewiesen, dass die Bildung von Salzsäure, Pepsin und Rennin auf die Fundusdrüsen (peptische Drüsen) mit ihren Belegzellen und Hauptzellen beschränkt ist.

Die Versuche ergaben, dass in Fällen von perniziöser Anämie Extrakte aus dem Fundusdrüsenabschnitt wirkungslos, solche aus dem sogenannten Kardiadrüsenabschnitt schwach wirksam, solche aus dem Pylorusdrüsenabschnitt stark wirksam und solche aus dem Duodenum ebenso stark wirksam waren. Die geringe Wirksamkeit des Kardiadrüsenabschnittes könnte auf die kleinere Zahl der Drüsen pro Oberflächeneinheit in diesem Teil zurückzuführen sein.

Verfasser schliesst aus diesen Versuchen, dass den sogenannten Kardiadrüsen, den Pylorusdrüsen und den Brunnerschen Drüsen, die hinsichtlich ihres anatomischen Baues fast gleich sind, auch die gleiche Funktion zugesprochen werden kann, wenigstens hinsichtlich der Bildung des antianämischen Faktors.

Dieses gesamte Drüsengebiet, für welches der Name Pylorusdrüsengebiet vorgeschlagen wird, ist der Sitz der Bildung des antianämischen Faktors. Diese Drüsen besitzen somit eine ganz bestimmte und lebenswichtige Funktion.

Weiterhin wird aus den Versuchen geschlossen, dass die perniziöse Anämie beim Menschen durch Atrophie und Inaktivität des Pylorusdrüsenabschnittes des Magens verursacht wird; somit haben die Versuche ausserdem den Entstehungsort der perniziösen Anämie des Menschen anatomisch festgelegt.

Experimentell dürfte sich die perniziöse Anämie vermutlich durch Exstirpation des Pylorusdrüsenabschnittes erzeugen lassen.

Es dürfte vorteilhaft sein, Magendrüsenpräparate zur Behandlung der perniziösen Anämie ausschliesslich aus dem Pylorusdrüsenabschnitt herzustellen.

THE researches about which I propose to speak have to do with the localization of the anti-anæmic factor (Castle's " intrinsic factor ") in the stomach.

In 1933, when we began our investigations, we had the following facts to go upon :—

We knew (Castle) that this substance was contained in normal gastric juice, we knew (Isaacs and Sturgis, Conner, Wilkinson) that it was contained in dried stomach tissue too, we knew (Castle, Wilkinson) that the substance was presumably

an enzyme, that it was not identical with pepsin or rennin, that it was of a different nature from the anti-anæmic principle in liver, but was basic to the formation of that principle, according to the diagram :—

enzyme————————certain components

in   in

stomach   food

The ultimate principle, resorbed from
the intestine and stored in the liver,
the kidneys, and the brain.

On the other hand, the immediate and most urgent question, as to what elements of the stomach produced this substance, had not been answered.

Some experiments (Isaacs and Sturgis, Conner, Wilkinson, Bondarenko and Dulcin, Burgess and Morgan) had aimed at finding out whether the substance was to be found in the mucosa or in the muscularis ; others (Henning and Stieger, Henning and Brugsch, Sharp and collaborators, Gutzeit and Hermann) endeavoured to determine whether it was in the fundus region or in the pylorus region.

The results were uncertain, and they disagreed, mutually, especially as to the localizing of the substance within the different gland regions.   It seems probable that faulty technique is to blame for this disagreement.

Our own investigations.—In our investigations we have assumed that the principle must be a secretion product—for it is contained in the gastric juice—and that a secretion product of so specific a biological character must be associated with certain cell-elements and could not be assumed to be secreted, so to say, diffusively from the gastric mucous membrane, which contains glands quite different in character.

We realized that the solution of the problem of localization required the fulfilment of two technical conditions.

In the first place, we had to be sure that the processes employed in our experimental preparations did not destroy the active principle, which is rather labile ; past experience (in this country, too [Wilkinson]), had shown that the gastric preparations sold commercially varied greatly in their therapeutic activity. For this reason, much experience and practice are necessary before an active and constant preparation can be produced, enabling one to make reliable experiments. We have had the advantage of such experience and practice through the Danish Medicinal Company.   This company has had four years' practice in the manufacturing of ventriculin Mco, and during four years' experience I have found that preparation to be nearly constant, both as to its anti-anæmic activity and as to its pepsin and rennin content.

Next, as the experimental preparations come from pig stomachs, we had to know all about the histological topography of that organ, so that we did not get the different gland-types mixed up in our preparations.   The fact is that the stomach of the pig has a most peculiar structure, and it is necessary to take this into account when excising material for experimental preparations.

Histological topography of the pig's stomach.—Consequently, our first task was an examination of the histological topography of the pig stomach, and I shall show how we (Meulengracht and Søeborg Ohlsen) have charted it by means of microscopical

examination of the stomachs of ten ordinary bacon pigs.   As a matter of fact, almost similar descriptions have been given in earlier literature (Mønnig, Trautmann, and others).

Even macroscopically the pig's stomach is seen to be divided as it were into three sections : a greyish, slightly folded cardiac region, a reddish, thicker, more

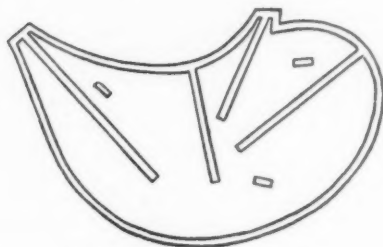FIG. 1.—Pig stomach, interior.

FIG. 2.—Microscoping diagram.

folded fundus region (in English = corpus region), and a smoother pyloric region, often slightly bile-stained.   At the cardiac orifice, stratified surface epithelium extends some way down over the stomach surface.[1]

We examined the stomachs by microscope, continuously along the curvatures, and continuously along the strips shown in the diagram.

[1] I am using Scandinavian and German nomenclature, which is not the same as the usual English nomenclature.   This may lead to some confusion, but I hope this will be straightened out in the course of my paper.

In type and appearance the various glands resemble the corresponding glands of the human stomach, but the grouping is quite different.

The conditions are best understood by examining the following three diagrams of mucosa in the so-called cardiac fundus and pyloric regions.

The so-called cardiac glands are more scattered and shorter than the other gastric glands. There is an abundance of interstitial tissue, which is rich in

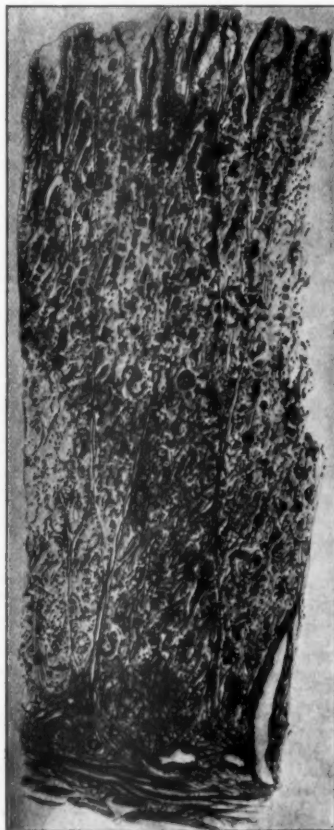   FIG. 3.—So-called cardiac glands.   FIG. 4.—Fundus glands (peptic glands).

lymphocytes, which again often collect in large lymphoid follicles. The glands are tubular, convoluted, and sometimes compound. The cell nuclei are fairly large, round or oval, and lie close to the base of the cell.

The fundus (peptic) glands are tubular, and, like those of the human stomach, closely packed in palisade fashion, with narrow septa and almost no interstitial cells. Lymphoid infiltrates are absent. The fundus glands have two well-defined

types of cell: oxyntic and chief cells. At the neck of the gland the oxyntic cells predominate, whereas at the base only chief cells occur.

The pyloric glands are alveolar-tubular, and the interstitial tissue is sparse. Downwards in the mucosa there are whole lobuli of glandular lumina, characterized by the large, clear pyloric gland cells.
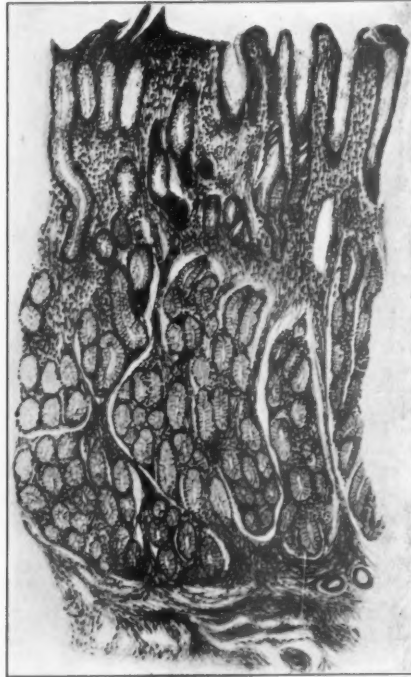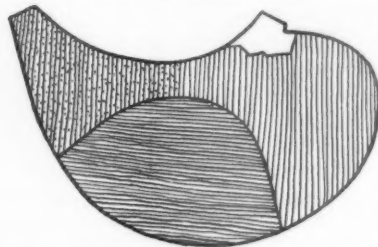

FIG. 5.—Pyloric glands.

FIG. 6.—Diagram of the topographical distribution of the various gland types in the pig stomach.

As the pictures show, the fundus (peptic) glands differ distinctly from the other two types by reason of their oxyntic and chief cells. On the other hand, actually there is considerable similarity between the so-called cardiac glands and the pyloric glands; the most marked difference is the greater amount of interstitial tissue in the

cardiac region, and the more massed quantity of glands in the pyloric region; the transition from the one to the other, however, is very gradual, and even the glandular cells seem very similar.

But we now come to the *topographical distribution of the various types of glands*, which was the chief object of our investigations.

The so-called cardiac region, as will be seen, occupies a considerable portion of the upper stomach. Just below the cardiac orifice the stratified surface epithelium extends from œsophagus down over the stomach wall, and comprises a belt of 4 to 5 cm. in width. But then the cardiac glands begin, and they extend along the lesser curvature almost to its middle, and along the greater curvature for as much as two-fifths of its length. Along the lesser curvature the cardiac glands and pyloric glands meet, but along the greater curvature the cardiac glands meet the fundus glands.

The fundus-gland region occupies the portion at the middle of the stomach; it does not reach up to the lesser curvature, as it lacks about one-fifth of the circumference. On the side of the stomach the fundus glands occupy a triangular area as shown on the figure. Measured along the greater curvature the fundus glands occupy two-fifths of it.

The pyloric-gland region occupies the remainder of the stomach, which means that along the lesser curvature the pyloric glands extend to about the middle, where
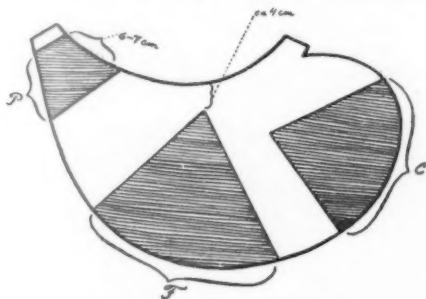

FIG. 7.—Our excision diagram.

they meet the cardiac glands, and along the greater curvature they extend as far as the fundus glands, so that they occupy the remaining distal fifth of the greater curvature. Brunner's glands only begin to occur at the pyloric sphincter itself.

As to the boundaries, these are very narrow. Along the fundus-gland region the boundary is only about ½ cm. wide (at the small curvature it is wider) but one of the reasons is that, histologically, it is much more difficult to distinguish between the two gland-types concerned—the cardiac glands and the pyloric glands.

For our purpose it is of great importance that the three gland regions are pure, i.e. the different gland types are not mixed up; except for the boundary areas there is only one type of gland.

As I have said, the macroscopic appearance gives us some guidance with regard to the position of the different gland areas.

We now wished to make experimental preparations of cardiac glands, fundus glands, and pyloric glands, and test their effectiveness on pernicious anæmia.

The distribution of the various gland-types in the stomach being what it is, we cannot simply divide the stomach transversely into three parts for our experiments, because the various types would then be mixed up in the preparations. We have therefore excised the material (mucosa + muscularis) for our preparations according to the diagram (fig. 7): from the cardiac-gland region along the triangle C, from

the fundus-gland region along the triangle F, and from the pyloric-gland region along the wedge P. The material is dried at low temperature, defatted and pulverized. The experimental preparations have been marked C, F, P: cardia, fundus, pylorus.

Before proceeding to discuss the clinical experiments I would say that we (Meulengracht and Schiødt) have been able to demonstrate, in a separate work, that the peptic and rennin activities were considerable in the preparations from the fundus-gland region, but slight in those from the cardiac and the pyloric-gland regions. We have also been able to show (Meulengracht and Søeborg Ohlsen) that after the injection of histamin immediately before the pig was killed, the gastric mucous membrane gave a positive Kongo reaction in the fundus-gland region but not in the other regions. I cannot go into these investigations here, but they demonstrate with sufficient certainty that *pepsin, rennin and hydrochloric acid are produced by the fundus-glands (peptic glands) and by them only*, and that, for that reason alone, the fundus-gland region can be proved to form a unit which in function differs from the rest of the stomach.
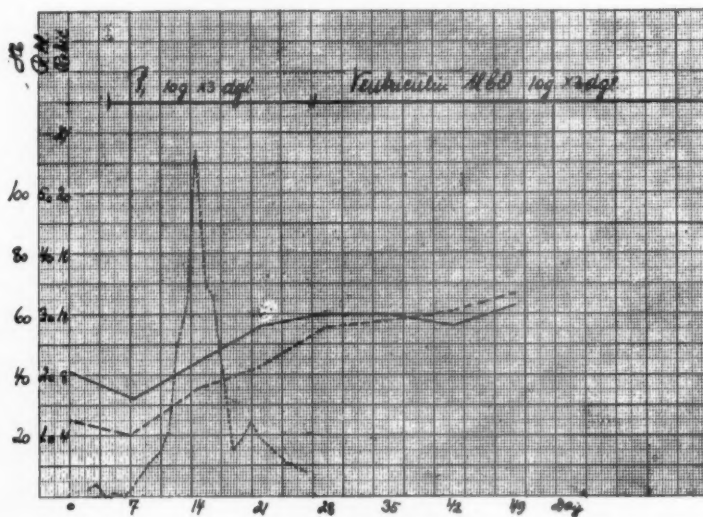
CLINICAL EXPERIMENTS.

A.—*Experiments with Fundus (= Corpus) and Pyloric-gland Fractions.*

Curve 1.

Experiment 1.—E. M. F. A., female, aged 65. Admitted to hospital 12.5.33.
Pylorus powder given, 10 g. three times a day, for an experimental period of three weeks. General condition quickly changed; reticulocyte reaction commenced on fifth day,


CURVE 1.—Case E. M. F. A.

reaching maximum on tenth day with 22%. Within the first four weeks Hb. and R.B.C. increased 30% and 2,000,000 respectively. After the three experimental weeks patient was put on commercial ventriculin, 10 g. three times a day.

Result.—Pylorus powder produced a typical and striking effect.

Curve 2.

Experiment 2.—F. S. H., female, aged 60. Admitted to hospital 14.8.33.

For an initial period of thirteen days patient put on fundus powder, 10 g. three times a day. In this period, and the next few days, no effect observed on reticulocytes, R.B.C. or Hb. General condition aggravated within the period. Treatment thereupon altered to
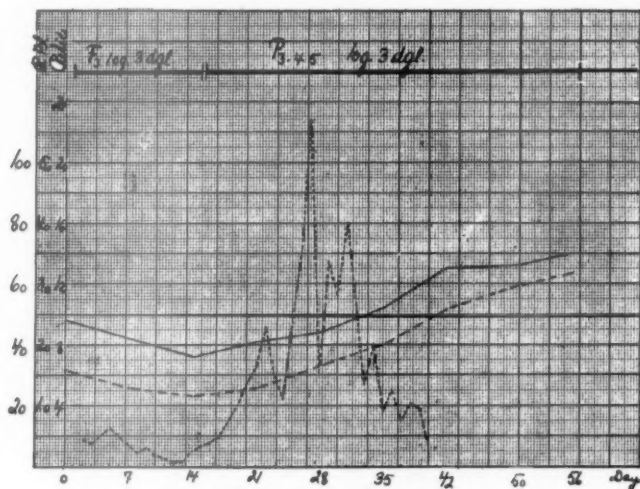
CURVE 2.—Case F. S. H.

10 g. pylorus powder, three times a day, whereupon the general condition quickly changed; reticulocyte reaction now occurred within eight days, with a maximum of 22·8% reticulocytes on the thirteenth day. Hb. and R.B.C. rise, the increase within the first four weeks being about 30% and 1,500,000 respectively.

Result.—No effect from fundus powder; typical and striking effect from pylorus powder.

Curve 3.

Experiment 3.—K. M. N., female, aged 44. Admitted to hospital 26.5.33.

For an initial period of seventeen days patient was put on fundus powder, 10 g. three times a day. General condition aggravated, no reticulocyte reaction, Hb. and R.B.C. fell. Treatment altered to pylorus powder, 10 g. three times a day. General condition improved within few days, reticulocyte reaction started on third day, reaching maximum of 26·4% on seventh day. Hb. and R.B.C. rose quickly; about 30% and about 2,000,000 respectively in the first four weeks.

Result.—No effect from fundus powder; typical and striking effect from pylorus powder.

Curve 4.

Experiment 4.—A. B. P., female, aged 62. Admitted to hospital, 21.8.33.

For an initial experimental period patient put on fundus powder for fifteen days, 10 g. three times a day. General condition aggravated, no reticulocyte reaction, Hb. and R.B.C. remained practically unchanged. Treatment thereafter changed to pylorus powder, 10 g. three times a day, whereafter there was an improvement in the general condition, a reticulocyte reaction, an increase of Hb.% and R.B.C., although both reticulocyte reaction and Hb.% increase were rather protracted. However, the improvement set in at a rather high level, namely between 50% and 60% Hb. and between 2,000,000 and 3,000,000 R.B.C. Under these conditions the effect is more protracted, because the height of the rise is, as is well known, in inverse proportion to the values of the Hb.% and the R.B.C.

Result.—No effect from fundus powder; typical effect from pylorus powder.
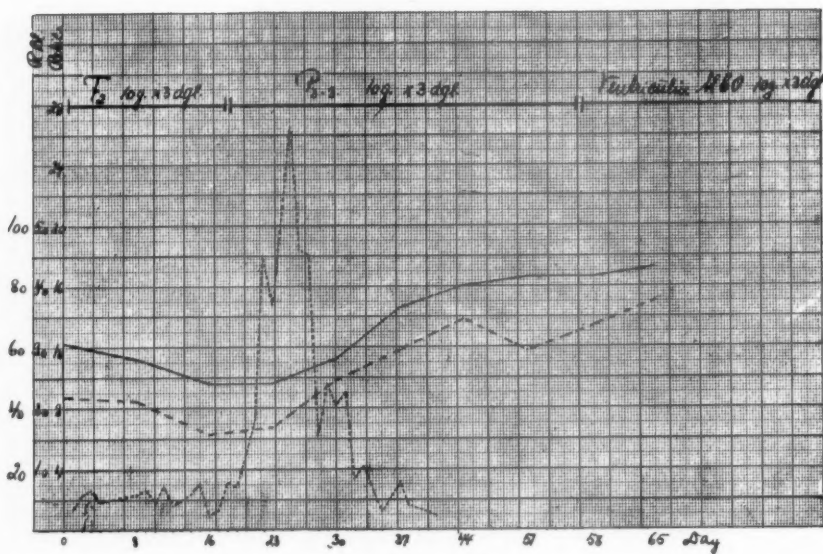
CURVE 3.—Case K. M. N.
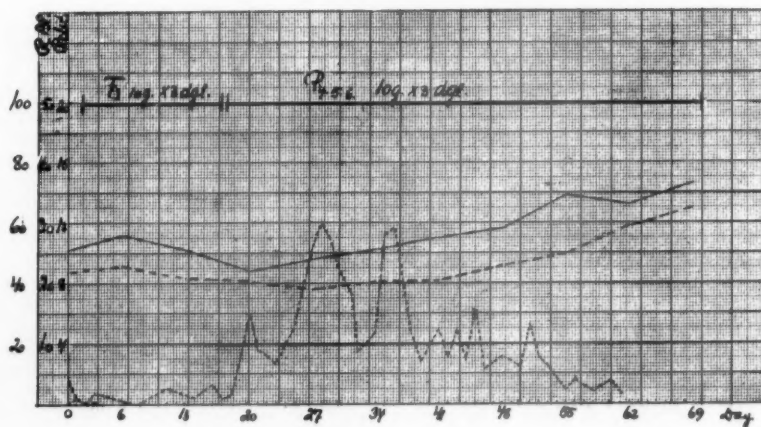
CURVE 4.—Case A. B. P.

Curve 5.

Experiment 5.—A. D. N., female, aged 55. Admitted to hospital 7.6.33.
Patient given fundus powder, 10 g. three times a day, for an initial period of six days
General condition became worse and the anæmia became so bad that the condition was
dangerous. The experiment had to be discontinued and patient was tided over with blood-

CURVE 5.—Case A. D. N.

transfusion and injections of hepsol. This was followed by a typical increase in reticulocytes
and a typical rise of Hb. and R.B.C. Finally, patient was put on ordinary commercial
ventriculin.

Result.—Fundus powder proved inactive within the experimental period, which, however,
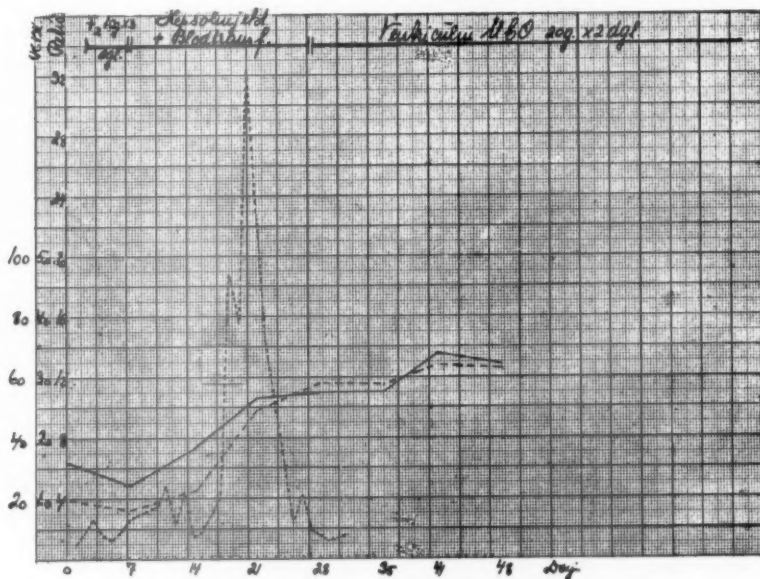was rather too short to permit of definite conclusions.

Curve 6.

Experiment 6.—A. K. W., female, aged 75. Admitted to hospital 2.11.33. In this
experiment patient was put on pylorus powder at once, 10 g. three times a day, and kept
on it for thirty-five days. There was a typical and pronounced reticulocyte reaction,
commencing on the sixth day and reaching the maximum of about 51% on the tenth day,
accompanied by a large increase of Hb.% and one of more than 2,000,000 R.B.C. within
four weeks.

Result.—Typical and striking effect of pylorus powder.

It appears from these experiments that there is a decided difference between
fundus powder and pylorus powder.

Fundus powder proved to be inactive in all experiments in which it was used.
This indicates that *the fundus glands* (*the peptic glands*), *consisting of surface
epithelial cells, oxyntic cells and chief cells, do not secrete the anti-anæmic factor.*
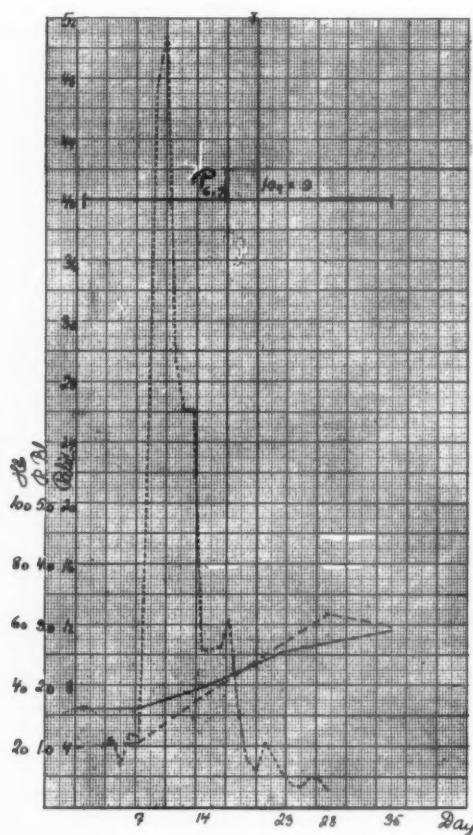
CURVE 6.—Case A. K. W.

On the other hand, in all the experiments in which pylorus powder was used it proved to be active, to a striking degree.   This means that *the pyloric glands, consisting of surface epithelial cells and pyloric-gland cells, secrete the anti-anæmic factor and that presumably this specific product is secreted by the pyloric-gland cells themselves.*

B.—*Experiments with Cardiac-gland Fraction.*

Now, however, we come to the question of the so-called cardiac-gland region with the so-called cardiac glands, which represent something characteristic of the pig stomach.   In man's stomach the so-called cardiac glands are reduced to a small, rudimentary area a few millimetres wide, up near the cardiac orifice.

I must say at the outset that the experiments with cardiac powder are more difficult to interpret than those with fundus powder and pylorus powder.   There are ten experiments in all.

Curve 7.

Experiment 7.—K. M. D., female, aged 46.   Admitted to hospital 10.4.33.   In this experiment the patient was put on cardiac powder, 10 g. three times a day, and this was continued experimentally for thirty days.   During the period there was an improvement in the general condition, and on the sixth day a reticulocyte reaction set in, attaining maximum on the eleventh day with about 40%.   There was an increase of 80% in Hb. and 1,500,000 in R.B.C. within the period.   This experiment would seem to show that cardiac powder is
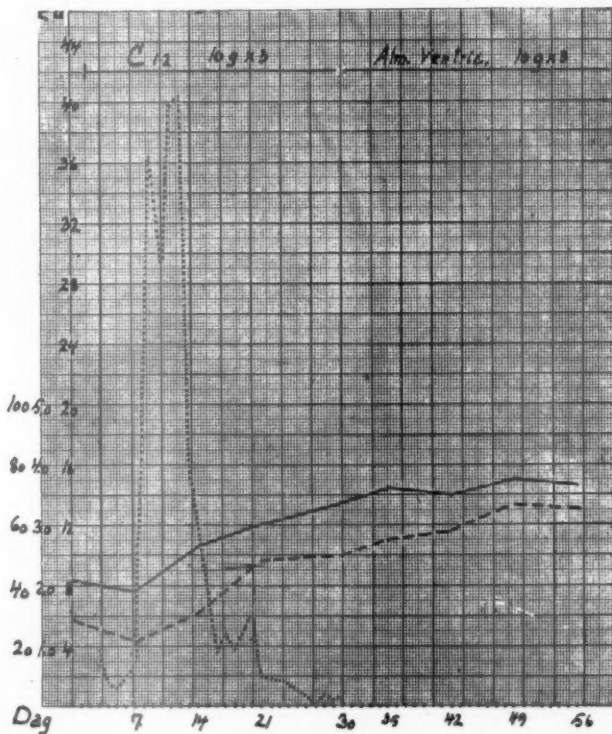
CURVE 7.—Case K. M. D.

exceedingly active, but unfortunately there is a defect that makes it very complicated : the patient had had her pernicious anæmia for five years, had neglected her treatment and was now very ill.   Fourteen days before admission to hospital she had taken to her bed at home and, as far as can be ascertained now, had taken three or four glasses of liver extract daily during the ten days before admission.   For this reason the reticulocyte reaction shown in the diagram may partly be the effect—somewhat tardy, it is true—of the liver extract.

Result.—Experiment defective and unsuitable for definite conclusions to be drawn.

Curve 8.

Experiment 8.—J. D., female, aged 53.   Admitted to hospital 6.11.33.
    This patient was put on fundus powder, 10 g. three times a day, for an initial period of twenty-one days.   In the early part of the period there was some slight activity in the reticulocytes, but the increase was less than 4%, such as may well be observed in patients with slight spontaneous reactions.   When the end of the experimental period came the

number of R.B.C. was still 2,000,000, as at the commencement. The slight increase of Hb. undoubtedly lies within the ordinary limits of experimental deviation. Thereafter patient was put on cardiac powder, 10 g. three times a day. No further reticulocyte reaction was observed, but there was a good increase of R.B.C., amounting to 1,200,000, within a month.
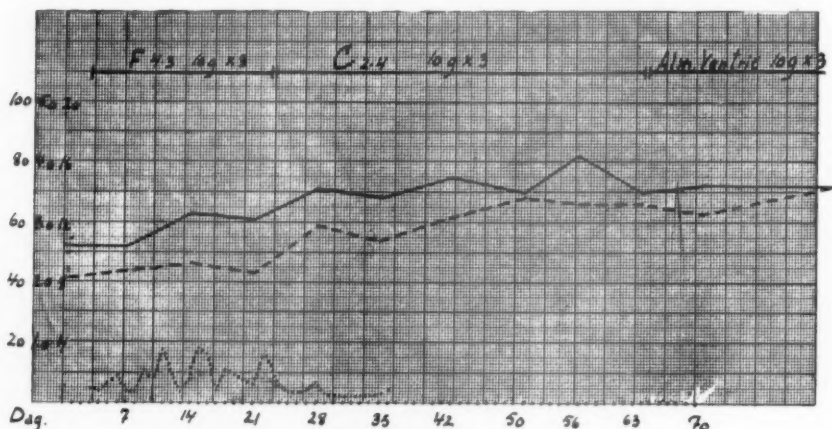
CURVE 8.—Case J. D.

Result.—Although there was no typical reticulocyte reaction, it would seem as if the cardiac powder had been active to some degree. As an experimental subject patient was not too suitable, as the starting point when the treatment began was rather high: about 2,000,000 R.B.C.

Curve 9.

Experiment 9.—T. A. F., female, aged 54. Admitted to hospital 3.11.33.

During a preliminary experimental period patient was put on fundus powder, 10 g. three times a day, for nineteen days. No improvement in the general condition; no increase of Hb. or R.B.C.; uncharacteristic activity in reticulocytes; no typical reaction. After the
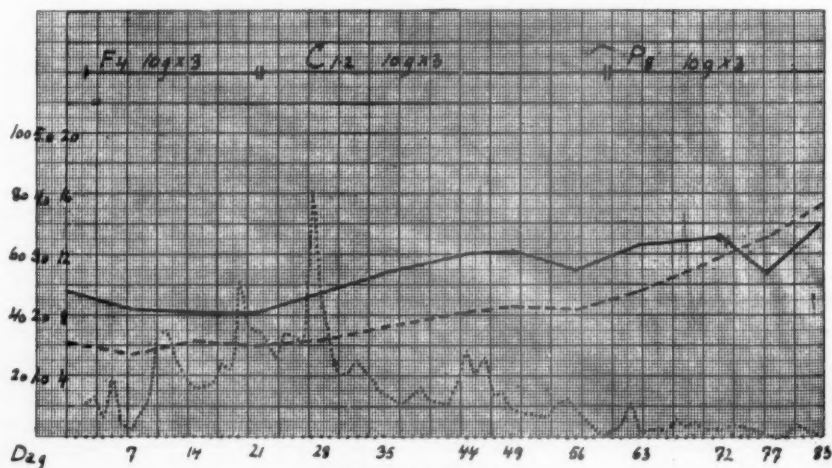
CURVE 9.—Case T. A. F.

nineteen days patient put on cardiac powder, 10 g. three times a day, when there was a renewed reticulocyte reaction up to 16%. At the same time Hb. and R.B.C. began to increase, but comparatively slowly. When later on patient was put on pylorus powder this increase became still more pronounced.

Result.—As regards the cardiac powder, my reading of the experiment is that it was active, but not so pronouncedly as with adequate treatment.

Curve 10.

Experiment 10.—H. M. A. W., female, aged 53. Admitted to hospital 31.1.34.

Patient was put on cardiac powder for twenty-seven days, 10 g. three times a day; there was a modicum of activity in the reticulocytes, up to $2 \cdot 7\%$ on the fifth day. No increase of Hb. or R.B.C. within the period, and no conspicuous change in the general condition. Thereafter patient was put on ordinary commercial ventriculin, 10 g. three times a day, after

CURVE 10.—Case H. M. A. W.

which there was again some reticulocyte activity, with an increase of up to $4 \cdot 3\%$ on the tenth day, and a distinct increase of Hb. and R.B.C.
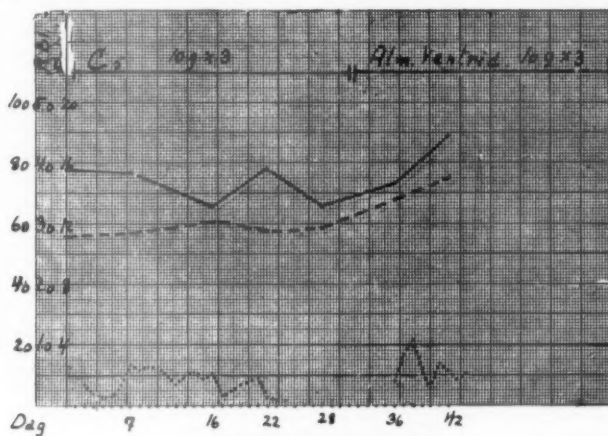
Result.—The cardiac powder cannot be said to have caused any typical effect, but the patient was not very suitable for experimentation, as the initial level at which the treatment was started was high.

Curve 11.

Experiment 11.—C. A., female, aged 64. Admitted to hospital 24.3.34.

For a period of two months patient was put on cardiac powder, 10 g. three times a day. On tenth day there was a reticulocyte reaction, with a maximum of $10 \cdot 4\%$. There was also an increase of Hb. and R.B.C., but the increase within the first month of the commencement of the treatment was only 17% Hb. and about 1,000,000 R.B.C. At the end of the experiment patient was put on commercial ventriculin, 10 g. three times a day.

Result.—The cardiac powder seems to have been active to some degree, though not so pronouncedly as with adequate treatment.

Curve 12.

Experiment 12.—E. P., female, aged 62. Admitted to hospital 30.3.34.

Patient given cardiac powder for seven weeks, 10 g. three times a day; on the eleventh day there was a reticulocyte reaction to a maximum of $13 \cdot 6\%$. There was an increase of Hb. and R.B.C., but it consisted only of about 17% and 700,000 respectively, in the first month. It should be observed, however, that the patient's anæmia was complicated with a slightly febrile, chronic bronchitis with bronchiectasis and chronic polyarthritis. After the seven weeks she was put on ordinary commercial ventriculin.

Result.—The experiment seems to indicate distinct activity from the cardiac powder, but not so marked as with adequate treatment.
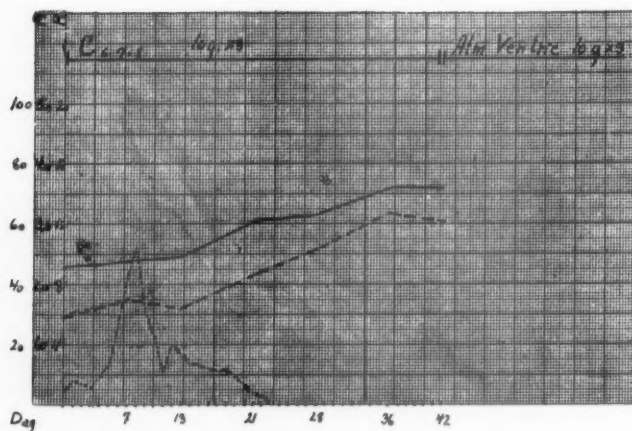
CURVE 11.—Case C. A.
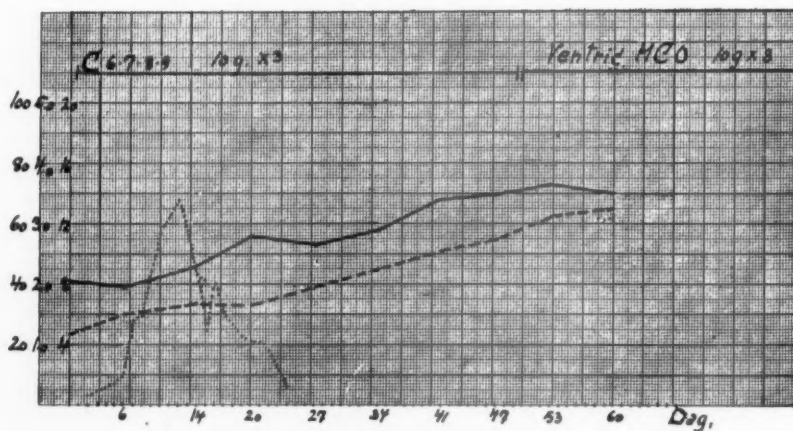
CURVE 12.—Case E. P.

Curve 13.

Experiment 13.—O. C. E. H., female, aged 48. Admitted to hospital 3.5.34.

For an initial period of eighteen days the patient was put on fundus powder, 20 g. twice a day, during which the general condition became worse; no reticulocyte reaction, and there was a drop in both Hb. and R.B.C. Thereafter patient was put on cardiac powder, 20 g. twice a day, under which a mild reticulocyte reaction set in, with a maximum of 3% on the seventh day; by this time, however, the anæmia had become so pronounced (Hb. 34%, R.B.C. 1,100,000) and the general condition so bad, that patient was given a blood transfusion of 500 c.c. After that there was again a slight reticulocyte reaction up to 6·2%. There was also some increase of Hb. and R.B.C. However, as the general condition was
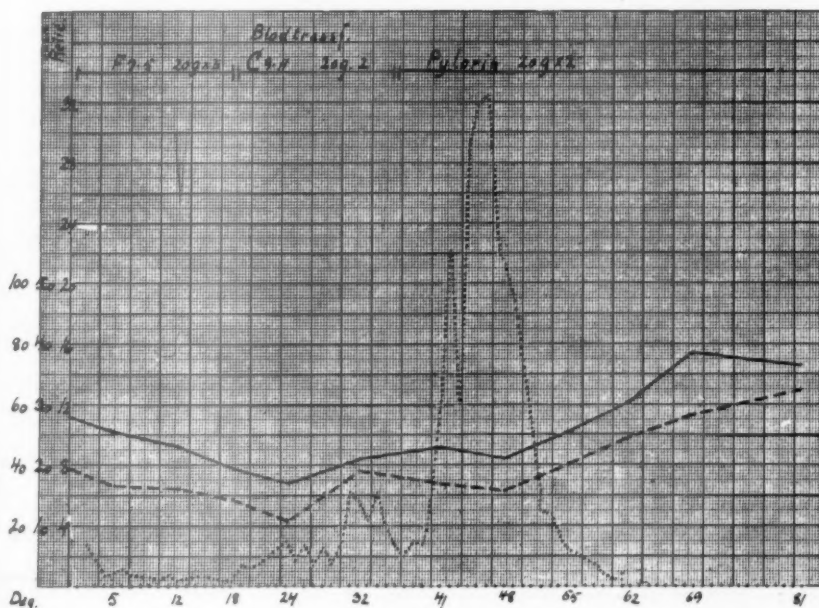
CURVE 13.—Case O. C. E. H.

still unsatisfactory, after a total of eighteen days on cardiac powder patient was put on pylorus powder (pylorin Mco), 20 g. twice a day. There was then a very marked reticulocyte reaction, up to 32·4% on the eleventh day, and at the same time a rapid improvement in the general condition and a brisk rise in Hb. and R.B.C. of about 30% and 1,500,000 respectively, within the first month of the commencement of the treatment. It should be observed that patient's perniciosa was complicated with an otherwise well-compensated myxœdema.

Result.—In this experiment there was no effect from the fundus powder, doubtful effect from the cardiac powder, and a striking typical effect from the pylorus powder.

Curve 14.

Experiment 14.—V. A. A., male, aged 37. Admitted to hospital 15.5.34.

In this experiment the patient was put on cardiac powder for a period of three weeks, 20 g. twice a day. A certain reticulocyte reaction was observable, with a maximum of 3·7% on the ninth day, but simultaneously there was an aggravation of the general condition and a

heavy fall of Hb. and R.B.C. to 22% and about 900,000 respectively. Blood transfusion was then resorted to, this being succeeded by a slight increase of Hb. and R.B.C. Then, after six days patient was put on pylorus powder (pylorin Mco), 20 g. twice daily, during which there was a vigorous reticulocyte reaction, up to 30·4% on the ninth day, a rapid recovery in
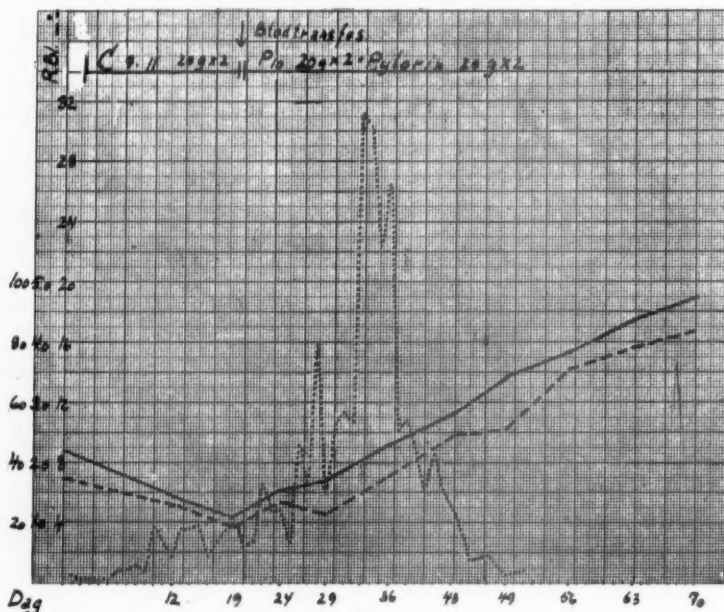
CURVE 14.—Case V. A. A.

the general condition, and a marked rise of Hb. and R.B.C. of about 30% and 2,600,000 respectively, within the first month.

Result.—No effect, or at any rate, a very doubtful result, from the cardiac powder, but striking and typical effect from the pylorus powder.

Curve 15.

Experiment 15.—V. J. R., male, aged 64. Admitted to hospital 30.5.34.

For a period of twenty-five days patient was put on cardiac powder, 20 g. twice daily. Throughout the entire period there was some activity in the reticulocytes, with a maximum of 6·6% on the sixteenth day, but without having the character of a reaction. Simultaneously there was an aggravation of the general condition and a fall of Hb. and R.B.C. Thereupon patient was put on pylorus powder (pylorin Mco), 20 g. twice a day, when a violent reticulocyte reaction set in, up to 25% on the eighth day; there was a rapid rise of Hb. and R.B.C. of about 40% and about 2,000,000 respectively within the first month.

Result.—No definite effect from the cardiac powder, striking and typical effect from the pyloric powder.

Curve 16.

Experiment 16.—M. O. N., female, aged 62. Admitted to Copenhagen Neurol. Dept. 14.4.34.

In this experiment patient was put on cardiac powder for twenty-two days, 20 g. twice a day, and there was a slight reticulocyte reaction up to 5·7% on the tenth day, but Hb. and R.B.C. remained more or less unchanged. Patient was then put on ordinary commercial ventriculin, 20 g. twice daily, whereupon there was a gradual rise of Hb. and R.B.C.

Result.—A faint, perhaps questionable, effect from the cardiac powder.
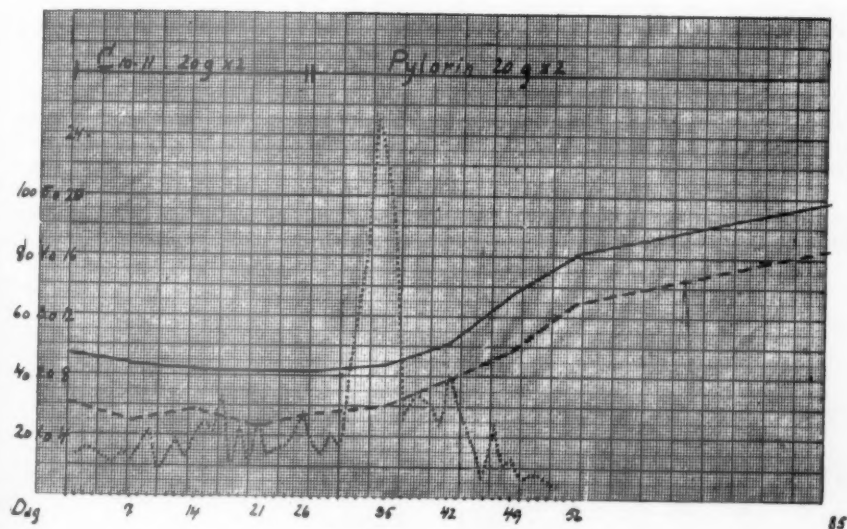
CURVE 15.—Case V. J. R.
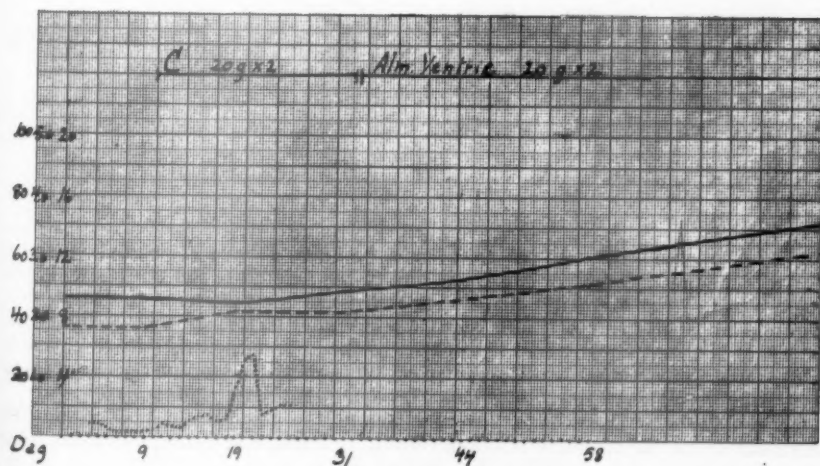
CURVE 16.—Case M. O. N.

As I have said, the experiments were not easy to read. They seem to show that *the cardiac region has a certain anti-anæmic activity, but this is slight, compared with that of the pyloric region.* The results of the experiments correspond to what happens when a treatment is given with insufficient dosage. The key to the interpretation of the experiments undoubtedly lies in the histological conditions.

The cardiac-gland cells themselves and the pyloric-gland cells are similar in appearance, as I have already said, and to my mind there is no histological reason for not regarding them as being identical. The differences that have been pointed out (Mønnig, Trautmann) are, I think, insignificant, and there are all forms of transition.

On the other hand, the cardiac-gland region and the pyloric-gland region differ in another point, namely in the relative volume of glandular substance per quadratic unit, as in the cardiac-gland region the interstitial tissue is more voluminous than in
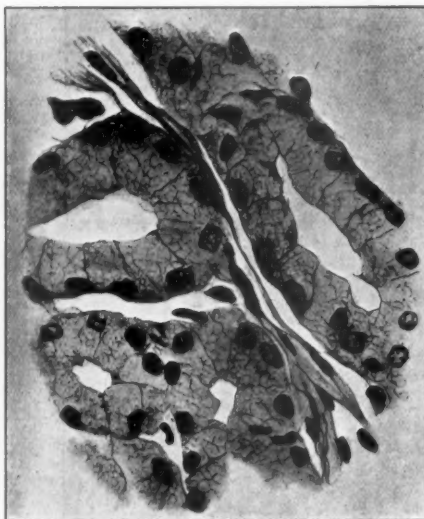
FIG. 8.—Cardiac-gland cells.   FIG. 9.—Pyloric-gland cells.

the pyloric-gland region, and consequently the glandular tissue itself is correspondingly smaller in volume. As far as it could be done, I have calculated that the relative glandular volume per quadratic unit in the mucosa of the cardiac region is from two to five times smaller than in the mucosa of the pylorus region, so that—accepting the identity of the two gland types—on account of this quantitative anatomical factor alone we might have expected the anti-anæmic activity to be much lower—three to five times—in the cardiac region than in the pylorus region. Exact figures cannot be given ; the proportions vary somewhat from place to place.

On the basis of these facts, let us examine the results obtained from the experiments. As we know, it has been shown by Minot and his collaborators that there is an inverse ratio between the number of erythrocytes at the beginning of treatment and the maximum of the reticulocyte reaction. This proportional dependence may be mathematically calculated, and Riddle has expressed it in a

formula, with the help of which it is possible to calculate with reasonable accuracy, in a given case, the probable reticulocyte maxima for oral liver extract treatment (extract = 600 g. of liver daily).

$$R = \frac{93.7 - 24E_0}{1 + 47E_0}$$

$$R = \frac{91.6 - 25.9E_0}{1 + 57E_0}$$

$$R = \frac{0.73 - 0.2E_0}{0.73 + 0.8E_0}$$
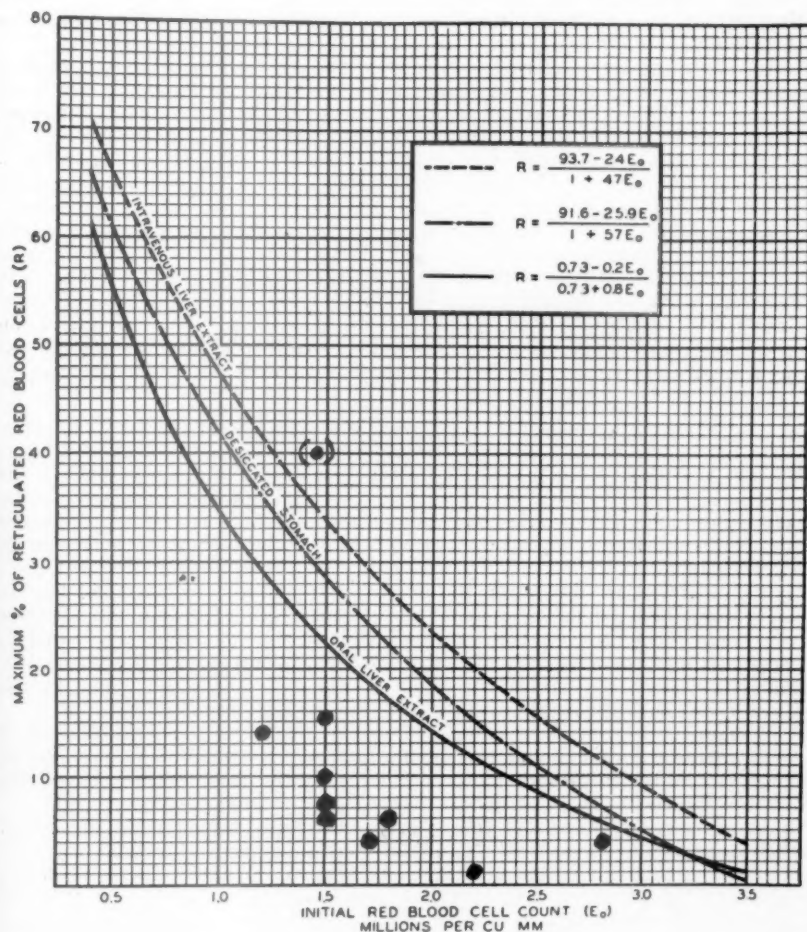
FIG. 10.—Bethell and Goldhamer's curve. Reticulocyte maxima for my cardiac-treated cases.

A corresponding formula, with table and curve showing the probable reticulocyte maxima with a given starting-point of red corpuscles, has been set up by Bethell and Goldhamer for treatment with dried stomach (ventriculin, 40 g. daily).

In this diagram the reticulocyte maxima found in my cardiac-treated cases are marked ●. Compared with Bethell and Goldhamer's curve, also shown in the diagram, they are much below the values to be expected from adequate ventriculin

treatment. If we imagine a curve (drawn roughly as well as it can be done) through the established values, and compare the two curves with the curves for various doses of liver as given in the paper by Minot, Murphy, and Stetson, we get an impression—a rough one, it is true—of the fact that the effectiveness of the cardiac fraction is from two to three times less than the effectiveness of the ventriculin (total stomach).

If we compare the smaller gland quantity per quadratic unit in the cardiac mucosa (three to five times less than in the pylorus fraction) with the lower effectiveness of the cardiac fraction (two to three times less than ventriculin made from cardia + fundus + pylorus), we shall see that, numerically, we are operating with differences of a corresponding size order, and that in so far there is nothing to prevent our assuming that *the lower effectiveness of the cardiac fraction is a function of the smaller gland quantity per quadratic unit.*

Consequently there is no reason, histological or functional, for not regarding the so-called cardia glands of the pig as being identical with the pyloric glands and as part of the same glandular system. In the pig this system extends in a remarkable manner from cardia to pylorus; in man it is otherwise, for the pyloric glands are localized to the region near the pylorus and extend merely a little way further up along the lesser curvature. In man, the so-called cardiac glands are represented only by a small rudimentary area, some millimetres wide, at the cardiac orifice.

C.—*Experiments with the Duodenum Fraction.*

Having got thus far, it naturally seemed important to us to extend the investigations to include Brunner's glands in the duodenum, which, histologically, very closely resemble the pyloric glands; apparently differing merely in lying under the muscularis mucosæ; many anatomists, in fact, consider them to be identical with the pyloric glands.

My own material for illustrating the anatomical conditions consisted of ten pig stomachs examined by Meulengracht and Søeborg Ohlsen; an examination was also made of conditions in the immediate vicinity of the pylorus. Furthermore, the duodenum was examined for a distance of 30 cm. in two cases. More complete anatomical investigations on the duodenum of the pig are to be found in the literature (*see* Ellenberger).

We have found that as we approach the pylorus from the middle of the stomach of the pig, the pyloric glands become more and more voluminous and lie more and more lobularly in the lower part of mucosa. Towards the pylorus the gland cells themselves gradually become larger, and rather lighter and clearer.

In the immediate vicinity of the pylorus the picture now begins to change. There the gastric surface epithelium, hitherto covering the surface and the pits, makes way for the typical intestinal epithelium with columnar and goblet cells. This intestinal epithelium covers the surface villi and the Lieberkühn crypts. At the same time the pyloric glands begin to disappear below the muscularis mucosæ, and very soon they lie entirely under it, spreading in large glandular lobuli, i.e. they now have the character of Brunner's glands, and here and there outlet ducts can be seen emerging from them up through the muscularis mucosæ and communicating with the Lieberkühn crypts.

In actual fact the cells of Brunner's glands are indistinguishable from the cells of the pyloric glands; they have the same large, clear, pale protoplasm, with some reticulation, and the same rather basally situated nucleus. If a single glandular lumen is examined in the microscope we are actually unable to say whether we are in the lower part of the mucosa, at the pylorus, or in the submucosa in the duodenum, i.e., whether it is a pyloric or a Brunner's gland.
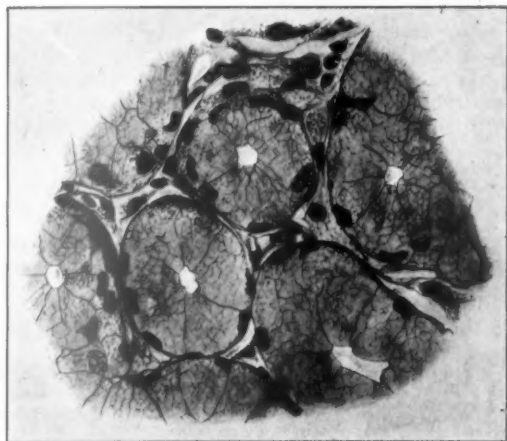
FIG. 12.—Brunner's gland cells.
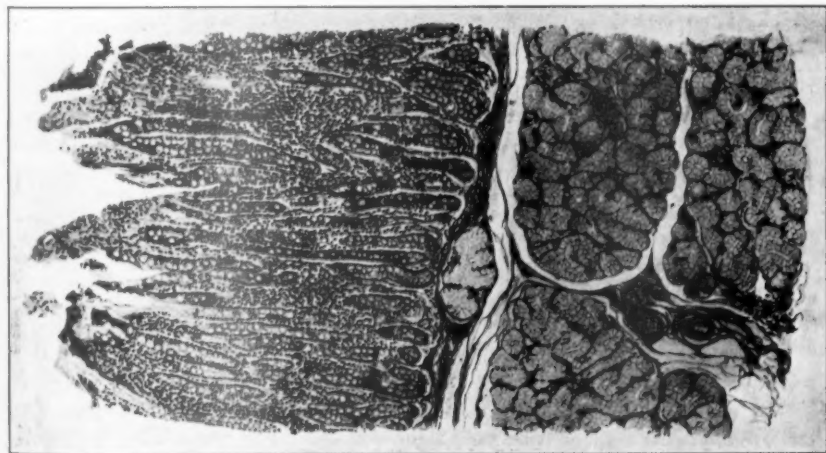
FIG. 11.—Section from mucosa and submucosa in the duodenum.

The volume of Brunner's glands is greatest just below the pylorus; there the glands spread in a thick layer everywhere in the submucosæ. Gradually as we get further down into the duodenum the volume becomes somewhat less, but even 20 to 30 cm. down in the duodenum there is still a thick and fairly continuous layer of Brunner's glands in the submucosa.

As I have said, we have not followed the glands more than 30 cm. down, as we had not secured more material. Ellenberger, however, states that in the pig Brunner's glands really extend three to five metres down the intestine, but in decreasing numbers, and lying more and more sporadically.

For making experimental preparations from the duodenum we took parts of the duodenum extending from 5 cm. to 15 cm. below the pylorus. This material was rather limited, the reason being that when we began we were not aware that Brunner's glands extended so far down the duodenum and so far along the intestine as they do.

Curve 17.

Experiment 17.—H. G. S., female, aged 47. Admitted to hospital 24.10.34.

In this experiment patient was put on duodenum powder, 20 g. twice a day. There was a rapid improvement in the general condition, on the sixth day a marked reticulocyte
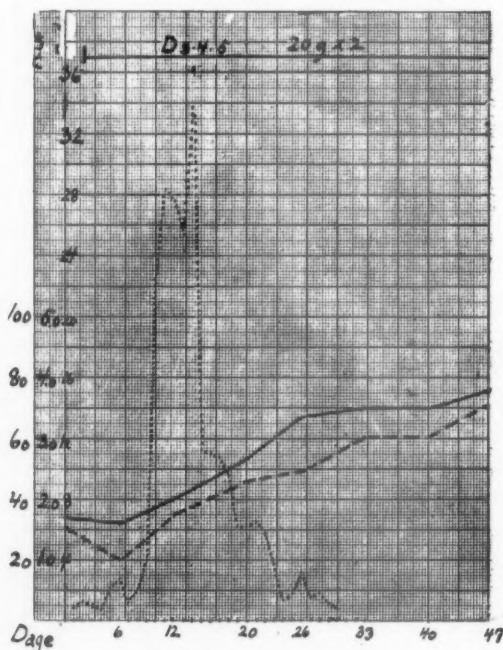
CURVE 17.—Case H. G. S.

reaction, reaching its maximum on the twelfth day with 34%. There was a pronounced increase of Hb.% and R.B.C.; 2,000,000 R.B.C. within four weeks.

Result.—A striking and typical effect from duodenum powder.

<div align="center">

Curve 18.

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·*Experiment* 18.—J. M. N., female, aged 60. Admitted to hospital 2.11.34.

Here the patient was put on duodenum powder, 20 g. twice a day. Under this treatment there was a rapid change in the general condition ; on the sixth day a reticulocyte reaction

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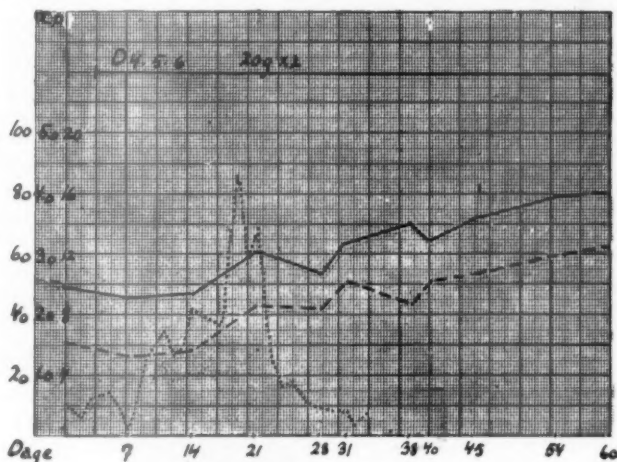
CURVE 18.—Case J. M. N.

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started, reaching a maximum of 17·7% on the sixteenth day. There was an increase of Hb.% and R.B.C. of 19% and 1,200,000 respectively within a period of about three weeks.

Result.—Again a striking and typical effect from duodenum powder.

In both experiments there was an extremely marked effect from the treatment with duodenum powder. The reticulocyte maxima correspond to Bethell and Goldhamer's standards for these maxima with adequate ventriculin treatment.

I have only notes of these two experiments here, but when I left Copenhagen I had two new patients on duodenum powder, and they reacted in the same striking way as those in the two experiments given here. I think the experiments show with sufficient clarity that *the anti-anæmic activity demonstrated as regards the pyloric glands also extends down into the duodenum.* Whether the anti-anæmic effect in the duodenum is associated with the intestinal epithelium or with Brunner's glands is as yet an unsettled question, but the anatomical similarity between the pyloric glands and Brunner's glands makes it most probable that the effect is connected with Brunner's glands. If this is correct, we are face to face with a fact of extraordinary importance ; theoretically, it means that *the pyloric glands and Brunner's glands may be assumed to be functionally identical and to belong to the same glandular system,* a system which in the pig extends right up from the cardia (the cardiac-gland region) down to the pylorus (the pyloric-gland region) and from there down into the duodenum and the intestine (the Brunner's-gland region).

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COMMENTARY

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If we now take the experiments all together, I think we may say that they decisively elucidate fundamental physiological questions, and that on important points they contribute to our understanding of pernicious anæmia in man.

Seen from a physiological point of view, *the experiments, so to say, give the pyloric glands a function.* As we know, it has hitherto been difficult to ascribe such a

function to the pyloric glands and the special pyloric-gland cells.   Now, after these experiments, it seems evident that *the pyloric glands are the bearers of a special secretory function and secrete the substance (Castle's intrinsic factor) that is essential to the blood and the nervous system, and is necessary to uphold life.*

Furthermore, the experiments show that the so-called cardiac glands, pyloric glands, and Brunner's glands, in the pig, may be assumed to be functionally identical, at any rate with regard to the anti-anæmic factor ; we might also express it this way : that in the pig the pyloric glands, or the pyloric-gland organ, have a remarkably large distribution, as over a wide area they spread up around cardia, proceed along the lesser curvature to the pylorus, and continue as Brunner's glands down into the duodenum and far down into the intestine.   Presumably there is a corresponding functional identity in other animals, but in those animals the pyloric glands have different distributions ; as a rule they are most concentrated round about the pylorus and, in the form of Brunner's glands, extend more or less down into the intestine, sometimes a long way.   In man, according to Buechner, Paschkis and Orator their distribution is as shown in the diagram.   Opinions differ as to how far down into the duodenum Brunner's glands continue (*see* Oppel and Ellenberger), but they appear to extend from 12 cm. to 15 cm. down, gradually becoming more and more sporadic.

Fig. 13.—Schematic diagram of gland regions in man (after Buechner).   C, cardiac ; F, fundus ; P, pyloric glands.

The experiments, compared with the earlier experiments of Meulengracht and Schiødt, also show that *functionally the pyloric glands are distinctly separate from the fundus glands (peptic glands), as the production of hydrochloric acid, pepsin and rennin is associated with the fundus glands, whereas the output of the anti-anæmic factor is a function of the pyloric glands.*

Now, if we examine these experiments from the angle of pernicious anæmia in man, we will find that they are of great importance to our understanding of that disease, for they, so to say, *localize it anatomically.*   As we know, in pernicious anæmia we have an atrophy and a secretory inactivity of the stomach.   It is diffuse in character, and comprises all the various glandular elements of the stomach, but in view of these experiments, it seems probable that *pernicious anæmia in man is caused by that part of the atrophy and inactivity that is comprised by the pyloric-gland organ,* that is to say it is due to the failure of a special function which must be localized there.   We have an analogy in the fact that diabetes is the result of atrophy and inactivity of the insular part of the pancreas.

This opens up the theoretic possibility that under certain circumstances pernicious anæmia may be due to an isolated atrophy or inactivity of the

pyloric-gland organ, without a simultaneous atrophy or inactivity of the fundus-gland organ, i.e. without simultaneous apepsia or achlorhydria (" dissociated achylia "), although judging from present clinical experience this possibility is of very small practical importance.

In our earlier work we had not investigated Brunner's glands. The present demonstration of the fact that Brunner's glands may be taken to be identical with the pyloric glands is a very important discovery.

I say this because it opens up the possibility of understanding: (1) Why every case of gastric atrophy with gastric anacidity does not lead to pernicious anæmia; (2) why every resection of the pylorus does not lead to pernicious anæmia. If we examine the diagram (fig. 14) of the probable extent of the pyloric gland region in man, which I have drawn approximately after Buechner, Paschkis and Orator, and of the Brunner's glands after Oppel and Ellenberger's textbooks, we realize at once that in both cases there is the possibility that a reserve of Brunner's glands in the duodenum can maintain the function.

Fig. 14.—Schematic diagram of the probable extent of the pyloric-gland organ in man.

Accordingly, the question of whether pernicious anæmia will develop under the circumstances I have named must be a quantitative one, depending upon the extent and functionability of the particular glands in the duodenum. To my mind a very important anatomical work would be the charting of the pyloric-gland in man on a quantitative basis.

An equally important pathologico-anatomical investigation would be that of the remaining parts of the pyloric-gland region in pernicious anæmia and other cases of achylia, as certain quantitative factors seem to come in here too. The topic has been touched upon in Faber and Bloch's famous researches on the digestive canal in pernicious anæmia (1904). They found Brunner's glands rather well preserved, but the work was not done along quantitative lines.

Again, these experiments open up the possibility of experimentally induced pernicious anæmia by means of suitable resection, i.e. resection of the entire pyloric-gland region, including Brunner's glands, from a suitable experimental animal, which means an animal whose pyloric-gland region is of such an extent that it is suitable for resection. I have the dog in mind in this connexion, for its pyloric-gland region (*see* Ellenberger) is so concentrated about the pylorus itself that a resection of it should be technically practicable. I may add here that the endeavours made hitherto by various research workers to produce experimental pernicious anæmia by means of gastric resection have failed, but those experiments were not based upon an elective resection of the pyloric-gland organ.

And finally, our experiments have opened the way for the manufacturing of more effective, and consequently pleasanter (smaller doses) therapeutic pig-stomach

preparations, a possibility which has already been exploited with much success in a preparation made from the pyloric-gland region of the stomach with the adjacent part of the duodenum.

BIBLIOGRAPHY

1 MEULENGRACHT, E., *Acta medic. scand.*, 1934, lxxxii, 352; samt *U. f. L.*, 1934, xcvi, 179.
2 MEULENGRACHT, E., and SCHIODT, E., *Acta medic. scand.*, 1934, lxxxii, 187; samt *U. f. L.*, 1934, xcvi, 187.
3 MEULENGRACHT, E., and SOEBORG OHLSEN, A., *Acta medic. scand.*, 1934, lxxxii, 384; samt *U. f. L.*, 1934, xcvi, 190.
4 CASTLE, W. B., and LOCKE, E. A., *Journ. Clin. Investigation*, 1928, vi, 2035.
  CASTLE, W. B., *Brit. Med. Journ.*, 1929 (June) (i), 1120.
  Id., *Amer. Journ. Med. Sci.*, 1929 (Dec.), clxxviii, 748.
  CASTLE, W. B., and TOWNSEND, W. C., *ibid.*, 1929 (Dec.), clxxviii, 764.
5 STURGIS, C. C., and ISAACS, R., *Journ. Amer. Med. Assoc.*, 1929, xciii, 747.
6 CONNER, H. M., *ibid.*, 1930 (Feb.), xciv., 388
7 WILKINSON, J. F., *Brit. Med. Journ.*, 1930 (i), 227.
8 MINOT, G. R., MURPHY, W. P., and STETSON, R. P., *Amer. Journ. Med. Sci.*, 1928, clxxv, 581.
9 MINOT, G. R., COHN, E. J., MURPHY, W. P., and LAWSON, H. A., *ibid.*, 1928, clxxv, 599.
10 RIDDLE, M. C., *Arch. Inter. Med.*, 1930, xlvi, 417.
11 BETHELL, F. H., and GOLDHAMER, S. M., *Amer. Journ. Med. Sci.*, 1933, clxxxvi, 480.
12 MORRIS, R. S., SCHIFF, L., FOULGER, J. H., RICH, M. L., and SHERMAN, J. E., *ibid.*, 1932, clxxxiv, 778.
13 WILKINSON, J. F., *Brit. Med. Journ.*, 1932 (i), 325.
14 BONDARENKO, E. A., and DULCIN, M. S., *Fol. hæm.*, 1931, xlv, 342.
15 BURGESS, J. P., and MORGAN, J. E., *Proc. Soc. Exper. Biol. and Med.*, 1931, xxviii, 371.
16 HENNING, N., and STIEGER, G., *Klin. Wchnschr.*, 1930, ii, 2145.
17 HENNING, N., and BRUGSCH, H., *Deut. med. Wchnschr.*, 1931, i, 757.
18 SHARP, E. A., McKEAN, R. M., and HEIDE, E. C. V., *Ann. Inter. Med.*, 1931, iv, 1282.
19 GUTZEIT, K., and HERMANN, J., *Münch. med. Wchnschr.*, 1931, lxxviii, i, 266.
20 WILKINSON, J. F., and KLEIN, L., *Lancet*, 1932 (i), 719.
21 MONNIG, G., "Zur Histologie der Cardiadrüsen von sus scrofa," *Inaug. Diss.*, Zürich, 1909.
22 TRAUTMANN, A., "Die embryonale und postembryonale Entwicklung der Cardiadrüsenzone im Magen von süs scrofa und : Sind die Cardiadrüsen in der Magen von süs scrofa Drüsen sui generis?" *Anat. Anz.*, 1925-1926, lx, 369.
23 ELLENBERGER, W., "Handbuch d. vergl. mikroskop. Anat.," Band 3, Berlin.
24 BUECHNER, "Die Histologie der pept. Veraenderungen und ihrer Beziehungen zum Magen-carcinom," Jena, Gustav Fischer, 1927.
25 Id., "Die Pathogenese der pept. Veraenderungen," Jena, Gustav Fischer, 1931.
26 PASCHKIS, K., and ORATOR, V., *Zeitschr. f. Anat. u. Entwicklungsgeschichte*, 1923, lxvii, 494.
27 OPPEL, A., "Vergleichende mikroskopische Anatomie der Wirbelthiere," Teil 2, Jena, Gustav Fischer, 1897.
28 FABER, K., and BLOCH, C. E., *Zeitschrift f. klin. Med.*, 1900, xl, 98.

Discussion.—Dr. C. C. UNGLEY : Professor Meulengracht's suggestion that the deficiency of hæmopoietin in pernicious anæmia is often quantitative rather than absolute is borne out by the results obtained with yeast. Experiments have shown that yeast owes its effect in pernicious anæmia, not to anything resembling liver active principle, but to Castle's extrinsic factor. For this reason a hæmopoietic response to yeast in cases of pernicious anæmia is of value in indicating that the digestive juices are not entirely devoid of intrinsic factor, and it is significant that, using large doses of yeast or wheat-germ, some degree of response was observed in ten out of eighteen cases of Addisonian pernicious anæmia [1]. In atypical cases of megalocytic hyperchromic anæmia yeast may be given as a diagnostic measure. A marked hæmopoietic response would suggest that factors other than defective secretion of intrinsic factor have contributed to the development of the syndrome. Such factors include defective diet, pregnancy, and interference with the absorption of hæmopoietic material from the intestine.

It is probable that the mechanism responsible for the development of subacute combined degeneration of the cord closely resembles that which gives rise to pernicious anæmia, i.e. that they are each the result of a nutritional deficiency conditioned by a gastric defect.

There is evidence that the effect of organtherapy upon the nervous system in subacute combined degeneration is not wholly the result of maintenance of the red blood-cell count at a high level, and that there may exist in liver and in brain a factor beneficial to the neurological phenomena distinct from that which influences the regeneration of blood [2]. The neuropoietic substance probably resembles the hæmopoietic principle in being a resultant of the interaction of two factors, intrinsic and extrinsic.

The dietary history of cases of pernicious anæmia with and without subacute combined degeneration fails to show extrinsic differences in the two groups. Nor does the secretion of

pepsin, chlorides, neutral red, or even of intrinsic factor itself as judged by the yeast response, yield any information which would indicate intrinsic differences.

On the other hand, there are certain facts which point strongly to the existence of a separate neural intrinsic factor. Firstly, there is the lack of parallelism of incidence and course between the anæmia and the neurological symptoms, and the existence of cases of subacute combined degeneration without anæmia. Secondly, subacute combined degeneration is extremely rare in those varieties of pernicious anæmia such as the tropical macrocytic anæmias and those occurring in sprue, cœliac disease and pregnancy, in which factors other than gastric defect contribute largely to the production of the syndrome. Such cases frequently show free acidity, a condition which has hardly ever been demonstrated in a proved case of subacute combined degeneration. Thirdly, there is, by way of contrast, the high incidence of subacute combined degeneration in cases of pernicious anæmia associated with gastric polyposis.

At the Massachusetts General Hospital, Boston, between 1927 and 1930, there were nine cases of benign adenomatous tumours of the stomach admitted. Six were in males and three in females, and the ages varied from 36 to 71, the majority being between 50 and 60 years of age.

Six of these nine patients had pernicious anæmia, with which was associated, in four instances, subacute combined degeneration of the cord. In three cases symptoms referable to anæmia preceded the onset of gastric symptoms, while in three others it was the gastric symptoms which appeared first. Subacute combined degeneration, when it occurred, was in each instance a later development. In one instance there was a history of alcoholic excess, but as a rule the past history contained nothing relevant. A significant family history was obtained in one case, the father having died of pernicious anæmia.

In one patient the polypi involved only the cardiac end and mid-portion of the stomach; there was no anæmia in this case. With this exception the pyloric end of the stomach was always the seat of polyposis, although in some instances there were polypi in other parts of the stomach. In four cases there was a single polyp, in three cases there were several, in one the polypi were very numerous (at least five), and in the remaining case the surface of the stomach was covered with small polypi.

Gastric analysis of the fasting juice and of a single specimen after a test meal was performed except in two cases, in neither of which was there anæmia. All seven cases showed an absence of free hydrochloric acid and the total acidity was usually low.

In two of the cases without anæmia the diagnosis rested chiefly upon the X-ray findings, which, however, were extremely characteristic. Radiographic evidence of polypi was confirmed at operation in five cases, and at post-mortem examination in one. The ninth case had a characteristic history and an extreme degree of pernicious anæmia. X-ray examination showed nothing of note, but when the patient died a year later, in a liver-induced remission, from thrombosis of the inferior vena cava, multiple polypi were found at the pyloric end of the stomach.

In one of the patients with subacute combined degeneration the degree of anæmia was not marked and no liver was given. She died at home eight months after leaving hospital and there was no autopsy. The remaining five patients with anæmia (three of whom had subacute combined degeneration) showed a characteristic response to liver, with a reticulo-cytosis and a rise of red blood-cells and hæmoglobin. The neurological condition has improved markedly in one case, and slightly in another, while the third died in a state of anæmia and advanced paraplegia due to neglecting treatment; the diagnosis was confirmed at autopsy. Of the two patients without subacute combined degeneration, one remained well for a year and died in a stage of liver-induced remission from thrombosis of the inferior vena cava. The other remains well as long as she continues to take liver.

Of the three patients without anæmia two were untraced, and the third died from coronary infarction soon after an operation to remove the gastric polyp.

The following case is of interest in that there was a change from nutritional (idiopathic) hypochromic anæmia to pernicious anæmia with subacute combined degeneration. Intensive treatment with liver extract brought about an improvement in the neurological condition which, however, was coincident with a return to a state of hypochromic anæmia.

The patient, a woman, aged 50, was first admitted to hospital in May 1929 with chronic hypochromic anæmia of three years' duration (R.B.C. 2,900,000 per c.mm., Hb. 80%, colour index 0·52, W.B.C. 6,600 per c.mm.). She was not seen again until January 1934 when she returned with typical pernicious anæmia and subacute combined degeneration (R.B.C.

1,200,000 per c.mm., Hb. 30%, colour index 1·25, W.B.C. 1,700 per c.mm. There was a histamine refractory achlorhydria. Following the daily intramuscular injection of liver extract there occurred a reticulocyte crisis reaching 26·2% on the eighth day, and a rapid rise of red cells to over 5,000,000 per c.mm. The injections of liver extract were continued and during the next seven months there was a progressive diminution of the symptoms and signs of subacute combined degeneration, including inability to walk, Romberg's sign, dysfunction of the hands, sphincter disturbances, paræsthesiæ, incoördination and loss of joint sense and of cutaneous sense. The red blood-cell count remained at over 5,000,000, but the hæmoglobin level never rose above 64%. By October 1934 she could walk normally and was free from paræsthesiæ or other nervous symptoms. Neurological examination was negative except for some residual hypoæsthesia and loss of joint sense in the toes and of vibration sense in the legs.

On the other hand, she complained of tiredness towards evening and showed marked ulceration at the angles of the mouth such as had occurred many years previously when she had first suffered from idiopathic hypochromic anæmia. Moreover the nails, which were coarse and brittle, now showed some spooning (koilonychia). Red blood cells numbered 4,500,000, with hæmoglobin 60%, and in stained blood-films the erythrocytes showed marked hypochromia.

The injections of liver extract were discontinued and she was given iron ammonium citrate 6 grm. daily. The hæmoglobin level rose promptly and reached 101% in ten weeks, with considerable subjective improvement. Three weeks after the commencement of iron therapy, however, paræsthesiæ reappeared in the lower extremities and although the numbness subsequently became less it has not yet disappeared entirely (twentieth week of iron).

This patient therefore showed multiple deficiencies. The deficiency of hæmoglobin-building materials was attributable to a poor diet, achlorhydria and slight repeated blood loss from hæmorrhoids. The later development of pernicious anæmia and subacute combined degeneration was probably due to impairment in the secretion of the intrinsic factor or factors in the gastric juice. With the appearance of pernicious anæmia, achromia was no longer apparent, possibly because the quantities of hæmoglobin-building material available were sufficient to supply the small number of red blood cells being put into circulation. But when liver extract was given the red blood-cell level rose to 5,000,000 per c.mm. and the deficiency of iron became once more manifest. It is noteworthy that the neurological condition improved coincidently with, and in spite of, the development of an iron-deficiency anæmia.

References.—1 UNGLEY, C. C., and JAMES, G. V., *Quart. Journ. Med.*, 1934, iii, 523. 2 UNGLEY, C. C., *Lancet*, 1931 (ii), 63, and 1932 (i), 227.

Dr. F. PARKES WEBER said that though the new data furnished by Professor Meulengracht suggested a plausible explanation for various atypical cases of pernicious anæmia, there still remained some clinical observations which were difficult to account for. As an instance he referred to the case of a woman, aged 38, in hospital under his care. She came with a macrocytic hyperchromic blood picture indistinguishable from a typical one of pernicious anæmia ; there was also a positive indirect Hijmans van den Bergh reaction in the blood-serum and the urine contained slight excess of urobilinogen, but there was no gastric achylia, fractional tests showing a normal amount of free hydrochloric acid. Wassermann and Meinicke reactions were negative. This case might have been explained according to Professor Meulengracht's data by supposing that Castle's "intrinsic factor" was absent or nearly absent owing to destruction of the pyloric glands in the stomach and Brunner's glands in the duodenum, though sufficient quantities of hydrochloric acid and pepsin were still being furnished by the main portion of the fundus (corpus) glands, which were not (presumably) destroyed. If this were so, however, the anæmia, one would suppose, ought soon to have yielded to ordinary doses of liver extract, such as had proved sufficient for the treatment of ordinary typical cases of pernicious anæmia.

The patient failed to respond to such doses (together with iron) and the anæmia increased. Owing to an exceptional agglutinating quality in the patient's blood-serum a suitable donor for blood transfusion could not be obtained. Then very high doses of liver extract were resorted to (intramuscularly, as before) and iron was continued, and the anæmia commenced steadily to diminish. Professor Meulengracht's data failed to explain why in this case larger doses of liver extract had to be given than in other (that is, in typical) cases of pernicious anæmia.

Section of Obstetrics and Gynæcology

President—EARDLEY HOLLAND, F.R.C.S.

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[*March 15, 1935*]

A Case of Obstructed Labour due to Radium Stenosis of the Cervix

By MARGARET M. BASDEN, F.R.C.S., F.C.O.G.

BEFORE describing this case of obstructed labour, I ought to explain that none of those responsible for dealing with it had any idea that the patient had ever suffered from carcinoma of the cervix or been treated with radium. She was very poor and a typical Cockney, and she apparently looked upon that incident in her past history as too trivial to mention to the district midwife with whom she had booked for her confinement. She was a multipara, aged 35, and had had six children, all with normal labours the youngest being four years of age. There had also been two miscarriages, but, none since the birth of the last child.

The radium treatment, of which Miss Hurdon will give the details, had been given two years before the present confinement.

She was admitted to the Mothers' Hospital, Clapton, in March 1934, from one of the hospital districts, with a history that she had a shoulder presentation, and that the membranes had ruptured two days previously. The liquor was stained with meconium and the fœtal heart could not be heard. There had been no definite pains. She was in poor general health, and had a very bad cough.

On admission.—The cervix admitted one finger only, and was not taken up. The membranes were ruptured and the child was dead. An attempt was made to perform an external version, but it was unsuccessful. I saw her four hours later ; she was then having good uterine contractions, although they were not painful, and I thought the best thing to do was to dilate the cervix manually under an anæsthetic, enough to bring down a leg. I expected this to be quite easy in view of the past history of six easy full-term labours. After trying for about an hour, I was able to squeeze three fingers into the os, but the cervix was still not taken up and felt very thick and unyielding and leathery, and it was quite impossible to reach a foot. At that stage I was obliged to go to another hospital, and I left the senior Resident Medical Officer to continue dilating the cervix, hoping that by the time I returned, a leg could be brought down. The patient's condition, however, gradually became worse, and the anæsthetic had to be stopped. So far as I remember, there was no bleeding at all during the manipulations. When I returned I found that the cervix had contracted down again to admit only two fingers, and there was œdema of the vulva and posterior lip of the cervix. It was then about 1.30 a.m. ; a small bag was inserted in the cervix and the patient was left alone for the rest of the night.

In the morning she seemed rather better, after a good deal of sleep with morphia, but the cervix could not be reached until an anæsthetic had been given, owing to the œdema, and the os was then found to be the same size as on the previous night.

At this stage a weight was attached to the bag, and the patient was given some anti-gas-gangrene serum as a prophylactic.

A puzzling feature of the case was that though there had been frequent long uterine contractions throughout the night, with definite relaxation between, no pains were felt by the patient, and more than once I wondered whether we had been mistaken in taking for granted that she was in labour, but I did not see how her symptoms, and particularly the increasing œdema, could have been otherwise explained. We waited until the afternoon but as there seemed by then to be no prospect of any further advance, I decided to perform Cæsarean hysterectomy. Miss Hurdon will show that Cæsarean section is the only treatment for labour complicated by radium stenosis of the cervix, but as I knew nothing about the previous radiumtherapy, and as the patient was a comparatively young multipara whose previous confinements had all been normal, I was extremely unwilling to undertake it.

I felt, however, that an attempt to perform embryotomy through such a cervix would be worse, and that classical Cæsarean section, apart from hysterectomy, might lead to fatal sepsis. I hardly think the child could have been delivered through a lower segment incision, and I did not consider it at the time.

Fortunately the operation was much easier than might have been anticipated, and the presence of the child in the uterus made very little difference to the hysterectomy. The patient eventually became quite well; I cannot say that she had a smooth convalescence, but this was partly owing to the presence of chest complications. She was given scarlatinal anti-toxin after the operation.

On opening the uterus afterwards, the child was seen to be lying in a right dorso-anterior position and so, even in an uncomplicated case, it would have been one of the more difficult types to deal with.

The patient has been kept under observation at the Marie Curie Hospital since her operation. Seven months afterwards a small recurrence of growth developed in the cervical stump, and she was admitted for further radium treatment. At the present time she is well and apparently free from further recurrence.

The Effects of Preconception Irradiation

By E. HURDON, M.D.

THE clinical history of Miss Basden's patient before her last pregnancy is as follows: In January 1932, three weeks after a normal period, there was a sudden severe hæmorrhage lasting only a few hours, and she was immediately transferred to the Metropolitan Hospital. I am indebted to the pathologist, Dr. Lucey, and the radiologist, Dr. Loughborough, for the following details :—

"On admission, the cervix was enlarged but there was no discharge; a piece was taken for pathological examination and 50 mgm. of radium was inserted into the uterus and left in for twenty-four hours. The pathological diagnosis was squamous carcinoma but the patient was allowed to go home for a week and as the hæmorrhage had stopped, did not return." The total dose, therefore, was only 1,200 m.e.h., a dose sufficient in this instance to keep the cancer quiescent for three years.

There was amenorrhœa for a year following the irradiation ; menstruation then returned and was regular until conception occurred in July 1933. The pregnancy proceeded normally to term, when the series of events reported by Miss Basden took place.

I first saw the patient in July 1934, three months after the Cæsarean section and subtotal hysterectomy. The cervical stump was small, nodular, fibrotic, and quite mobile. No change was noticed when the patient was examined again in August. In October there was no discharge but the cervix bled slightly. A fragment was taken with the punch for pathological diagnosis but showed only normal glands and slight inflammation.

In November, as there was still some bleeding I curetted and found squamous carcinoma. The patient refused to have treatment until after the holidays and was not admitted until January 1, 1935. Radium treatment was then given—three years after the first irradiation. The total dose given was 4,268 m.e.h. in three doses at six and fourteen days' interval—528 m.e.h. in the small cervical canal and 3,740 m.e.h. in the vagina. The screening was 1 mm. platinum in the cervix and the equivalent of 1·3 mm. platinum in the vagina, both with secondary screens of 1·5 mm. rubber.

In connexion with this case only cases of pregnancy following irradiation, especially irradiation for cancer of the cervix, will be considered. There are very few reports of conception subsequent to irradiation for cancer of the cervix. In a rather hurried search I have found only 12 cases. In six of these the patients were pregnant at the time the cancer was treated, the subsequent pregnancies occurring at periods of from two months to four years later. It is not very surprising that subsequent pregnancies should occur after irradiation of cancer of the cervix during pregnancy. Cancer complicating pregnancy is usually discovered early, the radium dose is generally small and, of course, no radium is placed in the body of the uterus; moreover the ovaries are a considerable distance away, and, as is shown in the following table, the majority of the patients were very young women.

PREGNANCY FOLLOWING RADIUMTHERAPY FOR CARCINOMA OF THE CERVIX.

No.	Author	Age	Ra. dose	Preg. after Ra.	Term	Abortion or premature	Mother	Child	Remarks
1	Gagey and Siredey, 1923	24	2,100 m.e.h.	2 years	Cæs.	—	Well 3 years	Normal	Adenocarc. of cervix. Irrad. preg. abort. after 6 weeks' ra.
2	Ikeda, 1927	—	About 10,000 m.e.h.	8 months	Spontaneous	—	Died hæm.	Normal	Irrad. during preg.
3	„	—	„	1½ years	„	—	„	„	„
4	„	—	„	2 years	„	—	„	„	„
5	Döderlein, 1928	31	2,510 m.e.h.	—	4th normal	3 aborts.	Well	Healthy at 8 years	—
6	Id., 1922	25	—	—	—	Abort.	Well 5 years	—	—
7	Schäfer	25	About 4,700 m.e.h.	4 years	—	Abort. induced	Well 5 years	—	—
8	Philipp, 1932	42	7,500 m.e.h.	2 years	Normal	—	Well	Normal	Irrad. preg. Abort. 6 months
9	Id.	25	8,800 m.e.h.	4 years	—	Abort. induced	Well 15 years	—	—
10	Wickham and Touflet, 1932	—	39 m.c.d.	1 year	Normal	—	Well at 4 years	Normal 3 years	—
11	Hofmann, 1934	—	2,040 m.e.h.	7 months	—	Vag. hyst. at 2½ mths. Growth	Well 2½ years	—	Irrad. preg. 1st child normal
12	Amalric, 1934. Clinical diagnosis	23	22 m.c.d.	3½ years	Morcellation	—	—	Stillborn	Morcellation after very long labour and death of child
13	Present case	35	1,200 m.e.h.	2½ years	Cæs. hyst.	—	Well	Stillborn	Obstructed labour

Records of many hundreds of cases of pregnancy following irradiation for non-malignant conditions are now to be found in the literature and a number of investigations have been carried out as to the effect of preconception irradiation on pregnancy and parturition and on the physical and mental development of the child. The animal experimentation relating to the effect on the offspring so far carried out, does not seem to have an important bearing on the clinical observations in human cases. The most important experimental observation with regard to preconception irradiation concerns the inheritance of various acquired radiation defects. The most important anatomical defect in human cases subject to irradiation has been micro-cephalic idiocy which is caused by the direct or indirect radiation of the fœtus and it is doubtful if it ever follows preconception irradiation. General constitutional weakness is difficult to attribute to a specific cause, but it is shown below that, as compared with the general vital statistics, the percentages of stillbirths and deaths under one year are not increased.

Murphy collected and analysed reports of 519 cases of pregnancy following irradiation and Flaskamp 245 cases. The analysis of the two series shows the following :—

Flaskamp's cases		Murphy's cases		Statistics for England and Wales 1933 Non-irradiated cases.	
Total pregnancies	245	Total pregnancies	519		
Full-term...	... 181	Full-term ...	... 402		
Stillborn ...	... 2·8%	Stillborn	0·9%	Stillborn ... .. 4·1%	
		Infant mortality	3·2%	Infant mortality 6·1%	

Murphy's series had 20% abortions and premature deliveries and Flaskamp's 30% ; general European statistics (non-irradiated cases) according to De Lee give 33% as usual ; there are no British or American statistics. Many of the abortions were induced on account of general conditions such as tuberculosis, syphilis or mental disorders. The few developmental defects showed no uniformity that might suggest a common cause. Martius thought the isolated case of microcephalic idiocy, reported by Gummert and Seynsche, might have been only a coincidence and that it was by no means clear that there was any relation between the condition and the preceding irradiation. These combined statistics of Murphy and Flaskamp include four of the cancer of cervix cases in my list. With few exceptions all the remaining cases were irradiated for metropathia hæmorrhagica, for fibroid tumours, or to produce sterility on account of some general condition. Doses of from 400 m.e.h. up to 4,500 m.e.h. were given for non-malignant conditions and from 2,100 to 10,000 or more for carcinoma, without producing sterility. Many had both X-rays and radium treatment.

The effect of preconception irradiation on the child is, as we have said, apparently negligible. With regard to the mother, a number—especially those previously treated for cancer of the cervix—have died from hæmorrhage during parturition ; obstructed labour due to stenosed cervix has occurred in cases following radiotherapy for menorrhagia, as well as after-treatment for cancer. In some cases the fibrosis was probably due to the interstitial insertion of needles ; in others the use of containers screened with only 0·5 mm. platinum and with no secondary screenage, or the very intensive dose given may have been responsible.

It is the custom at the Marie Curie Hospital, in treating non-malignant hæmo-rrhage or fibroid tumours, to place all the radium, which is screened with 1 mm. platinum and 1·5 mm. rubber, in the body of the uterus, filling the cervix with the empty cuff of the rubber screen. With this technique we hope to avoid injury to the cervix.

Conclusions.—(1) When pregnancy follows irradiation for cancer of the cervix,

delivery should always be by Cæsarean section, in the interest of the mother, and sterilization is advisable.

(2) Pregnancy following preconception irradiation for myopathia hæmorrhagica, fibroid tumours, or for sterilization, proceeds normally, and with few exceptions parturition is normal. When a stenosed, fibrotic cervix is likely to cause obstruction Cæsarean section should be performed.

(3) There is no definite evidence that preconception radiotherapy affects the child.

(4) Radiotherapy is not a perfectly reliable method of producing sterility.

REFERENCES

GAGEY and SIREDEY, *Bull. Soc. d'Obstét. et de Gynéc. de Paris*, 1923, iii, 168.
IKEDA, *Zentralbl. f. Gynäk.*, 1927, li, 407.
DÖDERLEIN, *Deutsch. med. Wchnschr.*, 1928, xlviii, 1997; and 1922, vii, 221.
SCHÄFER, *Verh. Deutschr. Gesell. f. Gynäk.*, 1920-21, xvi, 63.
PHILIPP, *Zentralbl. f. Gynäk.*, 1932, lvi, 1409.
WICKHAM and TOUFLET, *Bull. Soc. d'Obstét. et de Gynéc. de Paris*, 1932, xxi, 258.
HOFMANN, *Zentralbl. f. Gynäk.*, 1934, xxxii, 1891.
AMALRIC, *Bull. et mém Soc. de Radiol. méd. de France*, 1934, xxii, 119.
MURPHY, D. P., *Amer. Journ. Obst. and Gyn.*, 1929, xviii, 179.
FLASKAMP, "Röntgenschäden," 1930.
DE LEE, cited by Murphy.
MARTIUS, quoted by Flaskamp, p. 242.
GUMMERT and SEYNSCHE, cited by Flaskamp, p. 241.

Discussion.—Mr. L. C. RIVETT said that he had not seen a case of post-radiation pregnancy, but he had seen a case in which the patient was irradiated twice in the last ten weeks of pregnancy. The baby was delivered by Cæsarean Wertheim's hysterectomy and had two bald spots on its head. He had seen the patient and her daughter nearly twenty years later and both were alive and well.

Mr. CHASSAR MOIR said that a clear distinction must be made between radiation during pregnancy and pre-conceptional radiation. A study of the literature made it abundantly clear that when a fœtus was radiated *in utero* during the earlier part of pregnancy, there was a risk of causing grave developmental defects such as microcephaly. Many such cases had occurred when a patient suffering from irregular hæmorrhage had been treated by radiation of the ovaries. During the courses of treatment an unsuspected pregnancy had begun and the early embryo had thus been exposed to harmful radiation. It would appear that in such cases the risk of damage to the fœtus was so high that artificial abortion was fully justified. Radiation late in pregnancy did not, apparently, carry with it so grave a risk to the child.

Turning now to the question of possible damage to future offspring by pre-conceptional radiation, the position was much less certain. When one considered that radiation of the ovaries resulted in the riper follicles and ova being put out of action, it seemed reasonable to suppose that when at last the ovarian function returned and ripe ova were again shed, these ova might still be damaged although not sufficiently to prevent their fertilization. In other words, one could not assume that there must be a sharp line of division between the injured and uninjured ova. Many small-scale experiments, mostly by continental workers, had been carried out during the last twenty years. Experiments on rabbits, guinea-pigs, and mice, seemed, on the whole, to indicate that future offspring were less robust than usual, and some experiments indicated that the second generation was damaged to a greater degree and, moreover, was sterile. On the other hand, Murphy in Philadelphia had carried out a large-scale experiment on rats and could find no evidence of damage to offspring. Unfortunately Murphy had not widened the experiment to include animals other than rats, nor had he adequately described the condition of future generations of his experimental animals. Experimental evidence was thus conflicting. He (Mr. Moir) had started work of this nature some years ago in the Obstetric Unit of University College Hospital. He had succeeded in producing a temporary radium sterility in a large number of mice and had made records of the subsequent offspring. Unfortunately, a disease in the mouse colony destroyed most of his animals and he had only succeeded in rearing two mice (females) of the second generation

These animals were much smaller than the normal, and in spite of being mated with many different males, never became pregnant.

In applying this work to the human species, it would obviously require a great number of years to produce adequate statistical material. One early report was by P. Werner, who some six or seven years ago published details of about 100 cases. He believed that there was some evidence of damage by the pre-conceptional radiation. The speaker to-night had quoted other statistics, which went to show that the children were as normal as others. He (Mr. Moir), considered that the whole question was still an open one, but, having regard to the experimental evidence, he considered that it was at present quite unjustifiable to subject a woman of childbearing age to ovarian radiation until every other possible line of treatment had been tried.

The Birth of a Chimpanzee at the Zoological Gardens, London

By JAMES WYATT, F.R.C.S.

As far as can be ascertained, only two chimpanzees have been born in this country, the first, last year at the Bristol Zoo, when neither was the date of fertilization known, nor the birth, which occurred at night, witnessed, and the second at the Gardens of the Zoological Society of London on February 15 of this year.

In this latter case a careful watch has been kept during the pregnancy, labour, and puerperium, and as the chimpanzee is the most human of all the anthropoid apes, I thought that an account would be of interest to the Members of this Section.

The ape in question is, roughly, 12 years old; menstruation commenced at the age of 8, and has occurred regularly every twenty-six to twenty-eight days, lasting about four days.

Attempts were made to mate her with a mature male who has been in the Gardens for some years, but he was quite inactive, and it seems that many males kept in captivity are impotent.

The London Zoological Society, knowing that the male at Bristol was potent, purchased him, and commencing on June 11, 1934, he was placed with the female for three hours a day for ten consecutive days, during which time coitus took place two or three times each day. As the previous period had lasted from June 4 to June 8, we can say with certainty that fertilization must have occurred between the seventh and seventeenth day of the menstrual cycle, as no further menstrual loss occurred.

Towards the end of August some enlargement of the nipples was noticed, and the skin became more pigmented and greasy, and about this time she began to have curious fits of rage, in which she screamed, threw herself about and bit the skin of her arms and legs, at times making herself bleed. As it was thought that this condition might be due to some calcium deficiency, seven grains of calcium sodium lactate were given to her three times daily—with good results. For a time this was stopped but, as the fits returned, it was continued throughout the pregnancy.

Her diet consisted of fresh fruit and vegetables of all descriptions, and two quarts daily of guaranteed tubercle-free milk irradiated with ultra-violet rays.

She remained among her companions until the end of October, and was then placed in a special house, where conditions of warmth and humidity and control of the public could be more easily regulated.

The breasts began to enlarge at the end of December, and secretion could be expressed from them, and it is of interest to note that about this time she herself pulled on the nipples every day, one concludes, with the idea of preparing them

for future suckling. Abdominal enlargement was noticed from the beginning of November, i.e. the fifth month, but fœtal movements were not visible until ten days before birth.

From the report of the keeper, I think that labour commenced about 2.30 p.m., as at this time the animal became restless; at 3.30 p.m. there was a discharge of blood-stained mucus from the vagina, and at intervals of from seven to ten minutes labour pains occurred; this was evidenced by a change of position on to all fours with a lowering of the hind-quarters and obvious discomfort in the pelvis, as with each pain the ape passed her finger into the rectum or vagina—I take it with the idea of trying to remove the cause of the trouble.   At about 4.30 p.m., during one of the vaginal manipulations, she evidently broke the membranes, as a definite discharge of fluid came away.

I first saw her at 6.15 p.m.; the pains were then coming at intervals of five minutes and lasting about sixty seconds, and it soon became evident that the fœtus was slowly advancing.   At 7.15 p.m. the head commenced to show during a pain and the mother made attempts, by pulling on the scalp, to hurry matters up, but the keeper managed to distract her attention sufficiently with a piece of bread and butter, to prevent her damaging the scalp, which her nails were tending to do.   With three more pains the head was crowned and now the ape's fingers were passed right around the head, more or less as we apply forceps, and she rapidly pulled it out and then grasped the neck and extracted the body.

Directly she saw her offspring she was obviously frightened by it; she sprang to the upper shelf of her cage, thereby breaking the umbilical cord, and the youngster fell back into the straw and at once commenced to breathe and move its arms.   The mother for some ten minutes ran about in the upper part of the cage barking furiously, but gradually quietened down, and when, shortly afterwards, the babe began to whimper, she at first replied to it and eventually picked it up in her arms and carried it to the shelf, where she proceeded to clean and cuddle it.

She was considerably worried by the umbilical cord, which was hanging from the vagina, and kept making attempts to pull it out, but without success, as it had broken very close to the vulva, and eventually, to keep her quiet, the keeper had to take his chair into the cage and sit with her.

The placenta had not come away by next morning and, after talking with Dr. Vevers, I was prepared to give her some femergen tablets, but before I arrived, she had pulled out the remaining part of the cord with the aid of a piece of cotton-wool, and as it was evident that the placenta was now in the vagina, I hoped that it would come away when defæcation occurred.   It did not, however, so in the early hours of Sunday morning, the keeper, having disinfected his hands, managed to remove a piece of blood-clot from the lower part of the vagina; the placenta quickly followed and he was able to secure it.   It is in appearance very similar to that of the human being, and although it had been retained for nearly thirty hours there was no evidence of any decomposition, and it had no unpleasant odour.

The baby made no attempt to suck, so on Sunday morning it was put to the breast, and after a little encouragement took a feed and since then has fed every three or four hours.   One point of interest here is that after an interval of about ten minutes the mother changed the babe from one breast to the other.

The mother had no action of the bowels for the two days following delivery, and was lethargic and disinclined to eat; her temperature rose to 99·5° F. and I was, I admit, frightened of infection, considering her mixed manipulations during her labour.   Alophen pills, which she had taken during her pregnancy, were tried, but she would not swallow them.   She took a tablespoonful of syrup of figs on Saturday evening and a similar dose three times on Sunday, but without effect.   On Monday morning her keeper volunteered to give her an enema and this proved highly

successful, as an enormous stool was passed, followed by a rapid improvement of the general condition.

The breasts showed no evidence of filling until the seventh day, but as the infant seemed contented, no attempt was made to feed artificially; Professor Plimmer has, however, kindly carried out some estimations of the milk, in case this should become necessary. The figures are as follows:—

	3rd day	4th day	9th day
Water	88·35	88·75	88·95
Fat	3·75	2·09	2·34
Protein	2·17	3·41	1·40
Lactose and salts (by difference)	5·73	5·75	7·57

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Section of Otology

President—E. A. PETERS, F.R.C.S.

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[*February* 1, 1935]

DISCUSSION ON THE AFTER-TREATMENT OF THE RADICAL MASTOID OPERATION

Mr. H. V. Forster: In this discussion we are concerned with the after-treatment of a familiar surgical procedure associated with the names of such pioneers as Kuster, Bergmann, Stacke and Zaufal, though Mollison [1] has proposed the shorter title, Zaufal's operation.

Sir Charles Ballance perfected the treatment of the operation cavity by skin-grafting, and I think our discussion should begin with a consideration of the problem of dealing with the cartilaginous meatus. Is this to be left alone? Should a plastic be cut? Should a skin-graft be applied?

The proceedings of this Section show that cases exhibited by Sir James Dundas-Grant [2] demonstrate satisfactory results obtained without meatal plastic before the general adoption of plastic methods.

Bárány [3], in 1923, re-awakened interest in this subject. In that paper he stated that since the autumn of 1921 he had not, as a rule, cut a meatal flap. It might be argued, however, that his methods were not radical, because he preserved the remains of the tympanic membrane, rarely removing the malleus, though nearly always taking away the incus, and the Danish otologist Jessen [4] hailed the operation as the best of the conservative procedures since the work of Stacke. Knutson [5], also very familiar with Bárány's operation, which he modified, carried out a number of ordinary radical operations without cutting the external meatal tube. Finally, the situation is reviewed by S. H. Mygind [6] and the more frequent use of the plastic method is advised.

It will be agreed that variation is advisable in the preparation of our operation cavities. Those cases in which the cavity is surrounded by hard bone with a forward lateral sinus and in which long-standing disease has not burrowed widely or low down into the mastoid process do very well after a conservative splitting of the meatal tube without suturing or thinning of soft tissues and cartilage. A lightly filled rubber glove-finger may be used to give support. Graham Browne [7] advocates less drastic interferences in the cartilaginous meatus.

My own experience began chiefly under the guidance of otologists who prepared their cavities by turning upwards a meatal flap, according to Ballance's method, but without skin-grafting, and I doubt if a few of my cases done with the incision reversed—following Milligan's method—are any better than the others. After the writings of Bárány and Knutson were published, a plastic was omitted in some. The

first results were good, and it is gratifying to see the posterior wall of the meatal tube retract gradually and yield a smooth cavity. A single disappointment in an unsuitable case should not condemn this method, but after a failure I returned to the Ballance plastic. Disliking the reinsertion of gauze-packing, I was satisfied for a while by the so-called "ambrine method." The use of hard paraffin No. 7 at the first dressing and repeated after an interval justified this change. Many operators at home and abroad have spoken well of this method—Daure and Liebault, David-Galatz, and St. Gheorghiu [8], and also Millet [9], who used it, together with Carrel-Dakin irrigations through a tube passed down to the eustachian orifice.

Is it necessary to use any packing after the radical mastoid operation?

My colleague, Mr. John Roberts, who prepares the Ballance flap very carefully by thinning and using catgut holding sutures, tells me that he inserts no packing except just within the meatal entrance, and is quite satisfied, but it was perhaps unfortunate that the first case of my own dealt with in this way proved to be one of aplastic anæmia, and severe reactionary bleeding followed the operation; consequently I prefer the loosely packed glove-finger as a tampon which can be removed with the least discomfort, and whose support permits of conservative treatment of the meatal tube by simple splitting of the posterior wall. If we can avoid cutting the meatal branch of the posterior auricular artery, physiological conditions will have been further respected.

The American otologist John B. Rae [10] advocates the Y-shaped plastic of Siebenmann because it does not deform the meatal entrance. He employs a supporting pack but does not remove cartilage or use holding-sutures. The original Siebenmann flap, in fact, resulted in an unsightly meatus, but Neumann shortened the arms of the Y-flaps and did not remove cartilage. The lightly packed glove-finger must have been used as a support by many operators. I used to perforate the end, making small holes—not for drainage purposes, but so that bipp cream might be fed gradually into the cavity from the gauze filling which had been smeared with this preparation. I relied on drainage outside the walls of this device, because water and body-fluids are excellent lubricants for rubber, but Sir James Dundas-Grant has recommended the use of a loosely-filled rubber finger-guard perforated at the blind end to secure drainage inside the rubber channel.

How are we to treat the cavity after the first dressing? Gauze ribbon is unpleasant for the patient, both when applied and when removed, because it adheres, and expert assistance may not always be available for the redressings. Campbell Smyth [11] of Boston advocates filling the cavity with sterile vaseline twice a day. I believe it is rather too early at this stage to rely on powder alone. I have seen a case speedily relapse under boric iodine powder and saline irrigations (not carried out by the operator himself); the discharging cavity and post-aural fistula both recovering speedily under syringing with perchloride of mercury. Eusol syringing of the cavity, either at once or after a few days' rest, has good results. Solutions liberating chlorine are well-tried remedies [12]. Later, for the patient's own use, I prescribe mercuric chloride solution 1 : 4,000, made up adequately with sodium chloride and coloured with methyl violet. This is followed by alcohol drops, 60% —a combination suitable for home use.

We may rely on powder insufflation entirely—boric acid or boric iodine—when there is less risk of discharge increasing. In the later stages of after-treatment we may have to deal with prominent granulation-formation and make use of chromic acid or the silver nitrate bead. The general health influences considerably the health of the cavity. Jessen calls attention to the case of a medical student in which the cavity showed marked and resistant granulation formation, but after a

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CORRIGENDUM.

Vol. XXVIII, p. 236 (Section of Otology, p. 16).
Title of Case shown by T. A. Clarke, F.R.C.S.Ed. :—

For " Abscess of the Ear," read,
" Absence of the Ear."

course of general treatment, with regulation of the mode of life and the use of ultra-violet-light baths, healed quite well.

The factor of neglect is also one difficult to control; it naturally varies with the type of individual, his living conditions and the opportunity to attend for observation. The most dramatic example of neglect in my experience was an otherwise satisfactory radical cavity which became perfectly dry but was found to be occupied by a crawling mass of maggots.

Finally, a most important point is that after the radical operation, and the more the operator has endeavoured to be radical, epithelium should not be expected to cover bone from which it is separated in part of the cavity by only a delicate wafer of fibrous tissue. No wonder relapses are frequent. Peters pointed out some years ago, that it was very unphysiological to cover bone with a thin layer of epithelium and this was the reason for employing a thick graft of skin and subcutaneous tissues turned into the cavity from behind—a method which he and Richard Lake had evolved [13].

Campbell Smyth [11] of Boston devised an ingenious skin periosteal flap composed of the periosteal tissues overlying the mastoid and of skin from the posterior meatal wall. His success may have been largely due to the provision of a suitable bed for invading epithelium. Hollinger [14] once expressed surprise at the ever-recurring question of the suppuration and non-suppuration of the radically operated cavity. He called attention to the obvious fact that this cavity is lined by a scar which forms scales and that these must be removed from time to time or they become macerated and suppurate. Scar tissue is not normal tissue.

In relapsing cases if recovery is delayed we might employ some of the more unusual and novel remedies.

Insulin is recommended as an application to the lining of the cavity by Kolisch [15] who reports good results and explains how the glycogen content of epithelial cells may be increased as in the liver cells. Cod-liver oil mixed with a neutral base of paraffin has been recently suggested for wounds.

Skin-grafting.—The skin-grafted case needs careful observation, and in a series from the Massachusetts Eye and Ear Infirmary [16] where skin-grafting is chiefly employed, patients who neglected to return for observation showed cavities in which desquamated epithelium had become moist and melted away, and they finally turned up with red moist cavities showing circumscribed areas of exuberant granulations. On the other hand practically every patient who reported regularly had a good dry cavity. It is said that the hearing results are better after skin-grafting, though Andrew Campbell [17] believed that in some of his patients the hearing was worse because the epithelial inlay had been placed over the inner tympanic wall, and he thought that results were better when this region had not been grafted. Fraser and Garretson [18] appear to demonstrate better hearing in skin-grafted cases. A few cases—in a series by Fraser and Stewart [19]—in which serious post-operative complications developed could hardly be quoted in order to condemn the method unless they were compared with an equal number not skin-grafted, and the number prepared without skin-grafts is considerably less.

In the after-treatment of the radical mastoid operation the need for further operations is fortunately rare. The treatment of post-operative labyrinthitis, meningitis, and lateral sinus thrombosis belongs to the realm of early complications—as does facial paralysis, now more hopefully treated by the methods of Duel and Ballance. On the borderline of the field of complications we may have to deal with persistent giddiness which resists medical treatment, but Mollison's operation through the external semicircular canal has given a number of good results and is

attractive because of its simplicity.   Dan Mackenzie [20], however, warns the
student of otology that some cavities which persistently discharge become dry after
operation upon a diseased and neglected labyrinth.   Cysts may develop in operation
cavities.   They are sometimes alarming until distinguished from the lateral sinus or
the contents of the middle fossa.   Perhaps the treatment of persistent post-aural
fistulæ should come into our discussion.   Donald Watson [21] has turned the
fistulous track inside out, and Ormerod and others have closed it, using the
muscle-flap method of Kisch.   Douglas Guthrie [22] praises the fat graft in dry
cases in children.   Stenosis of the external meatus may call for plastic methods, but
an account has been published of at least one case [23] in which dilatation by
laminaria was successful where re-operation had failed.

There is also the problem of operation on the eustachian tube in cavities that
remain moist in the tympanic part.   Fraser [24] has stated that in his failures to
obtain a dry cavity the factor of chief importance was the inability to obtain closure
of the eustachian tube.   Next was faulty general health—and next, narrowness
of the external meatus.   In some cavities remaining moist in the tympanic
part, however, the lining membrane itself is at fault and not the eustachian
tube, as Keen [25] proved in a series of school-children.   Keen also found that such
cases constituted a group with poor hearing.   Viggo Schmidt [26], of Copenhagen,
has been able to cure persistent tubal suppuration by zinc ionization, employing a
negative electrode in the rhinopharynx.   No doubt Friel, Jobson, and other earlier
workers in our own country, have found zinc ionization useful for these cavities.
Simpler methods, however—such as silver nitrate solutions or the silver nitrate bead
which Millet [9] uses—appear to be successful at the tympanic end of the
eustachian tube.

Hearing.—Can we do anything to preserve or improve hearing in the radically
operated ear ?   Peltzer [27] remarks on the use of a prosthesis of gauze treated with
ointment.   Keen has shown how those cases with a moist tympanic lining, not
necessarily associated with a patent eustachian tube, do not transmit sound so well
as dry, delicately-lined cavities.   The dry, but rather thickly-lined, promontories
come next in hearing efficiency.   Cases with poor bone-conduction become steadily
worse, and it is the rule, apparently, when there is a sound ear on the other side, for
the more favourable cases—though improving for a time—to get worse from disuse
on the operated side.   If exercised, however, improvement may take place, as in
Keen's case of the boy who insisted on using the poor ear for telephone reception.
The problem is more serious when the hearing on the other side is poor, or when
both ears have been radically operated.   Keen [28] has written favourably of
the electrophonoide method of treatment for deaf children ; perhaps it will be of
use after the radical mastoid operation.   Some of Keen's cases were of this kind and
Cathcart [29] has reported a few successfully treated.   In a discussion held by this
Section last year, no agreement was reached, concerning the usefulness of this
instrument.   In the treatment of deafness after the radical mastoid operation its
value should be assessed on the practical results.

Theoretical anxiety that the ear may be damaged or fatigued by sounds used for
therapeutic purposes should not be influenced by our knowledge of the traumatizing
effects of industrial noises, to which noxious stimuli, according to Russian otologists,
the damaged or feeble ear is particularly susceptible.

When an audiometer is used as the source of transmitted sound in experimental
work it has been found difficult to fatigue the auditory end-organ or nerve when the
middle-ear structures have been damaged.   This has been demonstrated in the cat
by Hughson, Crowe and Howe [30] and in the human being by Josephson [31].
The subject, however, is a complex one, but has further interest when the question

is asked whether the use of an electrical aid to hearing may cause the residual hearing to depreciate further in a deaf person. Dr. Phyllis Tookey Kerridge [32] believes that this is not to be the case and has demonstrated by means of audiography that the threshold of hearing has been definitely lowered in one or two cases where these instruments have been worn. These findings are encouraging, even though in the cases described the patients had not undergone a radical mastoid operation.

REFERENCES

1 MOLLISON, W. M., *Journ. Laryng. and Otol.*, 1930, xlv, 95; *Proc. Roy. Soc. Med.*, 1929-30, xxiii, 381 (Sect. Otol., 1).
2 DUNDAS-GRANT, Sir JAMES, *Journ. Laryng. and Otol.*, xxxix, 452; *Proc. Roy. Soc. Med.* (Sect. Otol.), 1924, xvii, 73.
3 BÁRÁNY, R., *Acta Oto-Laryng.*, 1924-25, vii, 41.
4 JESSEN, JES., *ibid.*, 1931, xvi, 459.
5 KNUTSON, E., *ibid.*, 1925-26, viii, 199.
6 MYGIND, S. H., *Journ. Laryng. and Otol.*, 1932, xlvii, 297.
7 GRAHAM BROWNE, L., *ibid.*, 1930, xlv, 102.
8 DAVID-GALATZ and ST. GHEORGHIU, *Ann. des Mal. de l'Oreille, du Larynx du Nez et du Pharynx*, 1928, xlvii, 1122.
9 MILLET, *ibid.*, 1928, xlvii, 644.
10 RAE, JOHN B., "The Nose, Throat and Ear and their Diseases," Jackson, C., Jackson, C. L., and Coates, G. M., Philadelphia and London, 1929, p. 561.
11 SMYTH, CAMPBELL D., *Amer. Ann. Otol. Rhinol. and Laryng.*, 1926, xxxv, 442.
12 LAURENS, G., HUBERT, C., and GIRARD, L., *Ann. des Mal. de l'Oreille, du Larynx du Nez et du Pharynx*, 1928, xlvii, 894.
13 LAKE, RICHARD and PETERS, E. A., *Journ. Laryng. and Otol.*, 1924, xxxix, 457; *Proc. Roy. Soc. Med.* (Sect. Otol.), 1924, xvii, 77.
14 HOLLINGER, JACQUES, Trans. American Otol. Soc.; *Ann. Otol. Rhinol. and Laryng.*, 1930, xxxix, 884.
15 KOLISH, E., "Suppurating radical mastoid cavities," *Zeitschr. f. Laryng., Rhinol., etc.*, 1929, xviii, 315-327.
16 WHITE, LEON E., *Amer. Ann. Otol., Rhinol. and Laryng.*, 1928, xxxvii, 419.
17 CAMPBELL, ANDREW, *Journ. Laryng. and Otol.*, 1923, xxxviii, 471.
18 FRASER, J. S., and GARRETSON, W. T., *ibid.*, 1922, xxxvii, 275.
19 FRASER, J. S., and STEWART, J. P., *ibid.*, 1930, xlv, 112.
20 MACKENZIE, DAN, "Diseases of the Throat, Nose and Ear," London, 1920, p. 528.
21 WATSON, DONALD, *Journ. Laryng. and Otol.*, 1930, xlv, 193; *Proc. Roy. Soc. Med.*, 1929-30, xxiii, 397 (Sect. Otol., 17).
22 GUTHRIE, DOUGLAS, *Journ. Laryng. and Otol.*, 1928, xliii, 713.
23 BECK, O., Report of Austrian Otol. Soc., Jan. 31, 1927, *ibid.*, 1927, xlii, 699.
24 FRASER, J. S., *Brit. Med. Journ.*, 1926 (ii), 1154.
25 KEEN, J. A., *Journ. Laryng. and Otol.*, 1926, xli, 145.
26 SCHMIDT, VIGGO, *Acta Oto-Laryng.*, 1924, vi, 568.
27 PELTZER, F., *Journ. Laryng. and Otol.* (Abs.), 1926, xli, 333; *Archiv. für Ohren-Nasen- und Kehlkopfheilk.*, 1926, Band 114, Heft 3-4.
28 KEEN, J. A., *Journ. Laryng. and Otol.*, 1934, xlix, 782.
29 CATHCART, G. C., "The Treatment of Chronic Deafness by the Electrophonoide Method of Zund-Burguet," Oxford Medical Press, 2nd Ed., 1931.
30 HUGHSON, W., CROWE, S. J., and HOWARD, A. HOWE, *Acta Oto-Laryng.*, 1934, xx, 9.
31 JOSEPHSON, E. M., *Amer. Ann. Otol. Rhinol. and Laryng.*, 1934, xliii, 1103.
32 TOOKEY KERRIDGE, PHYLLIS M., *Lancet*, 1935 (i), 104.

Mr. C. Gill-Carey: I began to prepare for my task as second opener in this discussion by inspecting the unsatisfactory radical mastoid operation cavities at my clinic and by looking up the notes of cases in which a second radical operation had been performed. While many of these moist cavities were due to lack of continuity in after-treatment and could be corrected by local measures, there were others in which I felt that the fault lay in neglect of some step at the operation.

In operating on mastoids with extensive cellular development, it is easy to miss an infected cell, which may give rise to symptoms long after apparent healing. Mr. Forster has mentioned unsuspected labyrinthine suppuration as a cause for an unsatisfactory cavity. I have been struck by the excellent cavities seen after labyrinthectomy. I believe that this is due to the careful preparation of the tympanum which must be carried out before the labyrinth can be safely opened.

Failure to smooth out the upper wall of the cavity, combined with infected bone left at the upper end of the facial ridge, tends to cause adhesions and pocketing. Neglect of the hypo-tympanum and eustachian region was responsible for poor results in other cases. The extra ten or twenty minutes spent in making the cavity look like the pictures in a textbook, will save much time and trouble in the post-operative period.

The particular type of plastic operation on the meatus did not seem to influence the result, so long as the opening was large enough to allow easy inspection of the cavity during the healing period, and—perhaps more important—large enough for the patient to keep the cavity clean in the years to come. Given a satisfactory cavity during the immediate post-operative period—that is the first two or three weeks—it can be handled in a variety of ways. The final results are probably the same, but the methods vary in the amount of discomfort and pain caused. I have only tried that of leaving the cavity unpacked in one or two cases, and it seemed that I had to do more cauterizing than usual to reach the stage of a dry cavity. Firm daily packing with dry gauze has, I think, little in its favour. It is painful and therefore inefficiently carried out by the tender-hearted. The constant disturbance of the growing epithelium seems to delay healing. Ambrine or hard paraffin was satisfactory in that excessive granulations did not form and the dressings were painless. Fairly frequent dressings were needed on account of discharge and odour.

The use of bipp has many advantages in the radical cavity. The effect of retarding the growth of granulation tissue, which in my opinion makes bipp unsuitable for prolonged use after the simple mastoid operation, is, combined with the deodorant properties, of the greatest help in radical mastoid cavities. Careful folding of the bipped gauze and the application of vaseline to the meatal skin aid in making dressings comfortable. The greatest point in favour of bipp is that when it is used the cavity can be left undisturbed for a week or longer. It is usual to remove the packing at the end of the third week, filling the cavity with boric iodine powder if there is much discharge, or wiping out with alcohol if it is nearly dry. It is at this stage that the exuberant granulations may require destruction.

I was first attracted to skin-grafting as a method of diminishing the number of dressings and shortening the healing period. After about twelve years I still think that there are distinct advantages in the use of skin-grafts. I have found that successful grafts shorten the healing period by one or two weeks, and lessen the need for cauterization. On the other hand, I think that the grafted cavity is delicate and needs regular cleaning, to avoid ulceration of the thin epithelial layer. I should say that particular care is needed in fashioning the bony cavity to avoid covering areas of bone which are infected. Primary grafts have been used. Once the technique of cutting the graft has been mastered, and a satisfactory method of keeping the graft in good position worked out, no difficulty was found in getting it to adhere. It was found easier to place the graft on a mould of the cavity than to spread it on the bone and then pack.

Stent moulds were satisfactory but difficult to remove. Hard paraffin and gauze soaked in liquid paraffin were given up in favour of a pack of folded gauze treated with bipp. It was found that, while bipp acted as a deodorant and allowed the cavity to be left undisturbed for several days, it did not destroy the graft. Dressings could be done at weekly intervals, and at the end of the second or third week the packing could be omitted, further treatment consisting of either alcohol drops or boric powder. Although the immediate results were good, it was found that the grafted cavity was delicate, and that collections of hard wax were liable to cause ulceration of the thin scar.

Inspection of the cavity at intervals is particularly important in grafted cases.

Finally, I should like to stress the importance of late post-operative treatment. Instruction of the patient as to the importance of cleaning the cavity once or twice a week, and inspection by the surgeon once every six months, will save time and obviate the disappointment occasioned by a return of discharge after perhaps a period of years.

Mr. A. J. M. Wright said it was impossible to deal with the question of after-treatment without trespassing on that of operative treatment in regard to technique.

When he read the title of this discussion he felt doubtful whether by "the radical mastoid" one was understood to include the clearing-out of the tympanic cavity, with attempted closure of the eustachian tube. His own personal opinion was that such an operation was based on a fundamental misapprehension. He believed that the tympanum, if one excluded the attic, was a part of the body which had an amazing power of recovery, and the more one tried to clear it out and substitute something else, such as squamous epithelium, the more troubles one was thereby piling up in the after-treatment, apart from any question of the patient's residual hearing. This was not a new story, but its truth was only being gradually unfolded. The importance of preserving hearing in the only good ear made him doubt the wisdom of clearing out the tympanic structures in doing an operation in which, otherwise, such a clearance would be made. And he found that patients did much better when he was less radical in his procedure. For that reason, during the last six or seven years he had, in every case, endeavoured to leave the tympanum, excluding the attic, as far as possible uninterfered with. He had set aside Wednesday mornings in each week to see old cases, and since he adopted more conservative methods the former hour so occupied had been reduced to about ten minutes.

With regard to the after-treatment of these cases, he found that the greatest difficulty was in getting a satisfactory opening in the meatus ; he did not know how to keep the flap up in every case. Sometimes he tried stitching it up, and sometimes this was successful, but not always.

From the point of view of the patient it was important to use dressings which did not adhere. For a long time he had employed a strip of sterilized oiled silk, which he removed at the end of the first week, when the stitches were taken out. He then left the wound uncovered, without dressings. He regarded the drying of the part as a powerful factor in preventing infection.

Mr. Harold Kisch said he proposed to limit his remarks to the operation of applying a temporal-muscle flap. He had been carrying out that operation since 1928, and in 1933 he examined his figures, i.e. concerning 50 consecutive cases in which this operation had been performed five years before, i.e. in 1928. There had been no selection of the cases. They were chronic cases, some with polypi, and some with cholesteatoma and he had found that in 68% of them the cavity was dry, and had remained dry since shortly after the operation ; 67·5% of the patients had improved—some greatly improved—hearing, in no case was the hearing worse afterwards. As to whether the patients were satisfied with the operation, the answer was Yes. In 32% the part was not dry, but in all of those the discharge had greatly diminished, and in most of them there was so little moisture that the discomfort was slight. Those available in the latter category were taken in hand, and with after-treatment of granulations by silver nitrate, dryness was secured in a few days.

The hearing results after this procedure were better than he had seen after other methods. In all the cases the bridge and incus were removed, in some the malleus also. Care was taken not to interfere with the rest of the middle ear; the eustachian tube was not touched, and the rest of the membrane was left behind. The fact that the inner wall was not touched and that of the rapid healing were reasons why the hearing was improved.

At various times he had been asked questions about this technique, and he would take this opportunity of answering some of them.

(1) Why put in a graft? Because by obliterating the mastoid cavity with living muscle, healing took place, and as there was no cavity to drain, no plastic operation on the meatus was needed.

(2) How was the muscle-graft introduced into the cavity? By separating the graft above and behind. The flap was left attached in front. The tongue of muscle was held, and by nicking intramuscular septa one could gradually pull down the muscle so that it lay flaccid in the cavity. This was important. The test was to replace the pinna in position, and if it were flaccid there was no tendency for the graft to rise. One must continue dissecting it down until that condition was obtained.

(3) Was there ever suppuration after the operation? Occasionally a hæmatoma formed in the region of the temporal muscle, and that might suppurate. The treatment then was to syringe out the cavity. He had never had to remove a graft even when a hæmatoma had formed.

(4) Were special instruments required? No, only ordinary simple instruments were necessary.

(5) When should it be done? In all cases of chronic suppuration; he did not do it for acute conditions. In cases of acute suppuration, if a large cavity were left, it could be filled later with a graft. In that case the bridge need not be removed. The operation was also useful for closing post-aural fistulæ. One could dissect up skin flaps, remove the lining of the fistula, and bring down the flap. After using this muscle-graft method for six years he considered that it obviated many of the problems which had been discussed by the openers to-day.

The President said that all would agree as to the necessity of keeping mastoidectomy cases under observation. Each used his particular method of post-operative treatment. He himself cut out a slot from the meatal sleeve by inserting Kocher's forceps and chipping out the endal fragment; it was a very rapid and accurate method of removing a piece of the tube. The meatus was expanded by means of the finger, permitting of the insertion of a rubber tube the size of a finger into the antrum. The tube was left in for a week, and it was possible to pack lightly and painlessly with bipp gauze by fixing the rubber tube with forceps. If the cavity was small it was not necessary to graft or to bring down a flap. If, however, the cavity was large, much time was saved by employing Kisch's muscle-graft, or the flap which Mr. Lake and he (the speaker) had described. After each of those measures the results were good. In the early stages he used bipp packing through the rubber tube. One could dress the ear even of a small child in this way, causing only slight discomfort. In later stages he had found iodine powder very useful.

Mr. Eric Watson-Williams said that he regarded the radical mastoid operation as one in which the tympanic contents were cleared out. If the operator left behind the membrane, with or without the malleus, that could not be called the radical mastoid operation; it was a compromise between a Schwartze and a radical

operation. He was becoming more and more reluctant to do the standard radical operation, especially in a patient with a quiescent ear, or in a case in which there was anything like useful hearing. When a radical operation had to be done, it should be a genuine radical one. His own practice was to use a wide plastic operation and then a skin-graft in a chronic case, using bipp packing. A subsequent dressing which had not been mentioned was glycerine. He found that glycerine, with 10% of ichthyol, was very comfortable for the patient; it was also cleansing, and was the least unpleasant dressing to have removed. He did not experience much trouble from exuberant granulations, or continued discharge from a cavity, except where a little mucous membrane had been overlooked at the operation. Most of the troubles following a radical mastoid operation were due to a patch of mucous membrane having been left, perhaps behind a bridge of scar tissue, where it was able to continue secreting mucus and persist beneath this protecting film. On the occasions when he had had old operation cases sent back to him with what were described as "granulations," it was simply that there had been left a patch of mucous membrane, possibly quite small at the time of the operation, but which owing to its protected position had been able to win the battle against the squamous epithelium and was, when seen again, briskly secreting. If one destroyed such a patch by cauterization and used every effort to keep the cavity dry, the condition, in nearly every case, cleared up. It was not carious bone, but patches of mucous membrane, which caused this later trouble.

He agreed with those who insisted on the necessity of keeping the cavities clean. It was disappointing when a patient returned with a complete cast of the cavity firmly wedged in position, with macerated epithelium beneath, but if there was no mucous membrane beneath, in such cases healing took place in a few days following the application of some antiseptic ointment.

A difficult problem was what one should do in the case of a fistula. He thought that the correct proceeding was at once to perform vestibulotomy and clean out the fistulous part of the labyrinth, not only because there was a better chance for a clean, dry cavity, but also because there was then no likelihood of vertiginous attacks, of which patients sometimes subsequently complained. He had done that only twice, and the results in both cases were good, yet his courage had failed, even subsequently, when he had been confronted with an apparently living labyrinth but with a fistula of the canal, for he did not like to risk opening the vestibule if it was not absolutely necessary.

Mr. J. F. O'Malley said that in these cases the surgeon was confronted with difficulties—on the one hand, of preventing the healthy tissues of the meatus from closing down and healing too rapidly, and, on the other, of getting the tissues in the infected cavity to heal. It seemed to him that the only reason the cavity did not heal was that there still remained some osteitis. Until there was some easily applied test by which it could be demonstrated that a spot of osteitis still persisted, the difficulties would continue.

For some years he had been disappointed with the radical mastoid operation, because he had operated on the assumption that there was gross middle-ear trouble fed by mastoid disease. On opening several mastoids he had found sclerosed bone, and consequently had to recognize that the middle-ear cavity, with its granulations and defective hearing, was the source of the trouble. He therefore thought of trying the converse method, attempting cauterization of the area, and seeing what could be done with the tympanic cavity and the aditus. Many of his cases had responded admirably. He applied a roll of wool with the applicator until the area of granulation tissue was white and shrunken. When this was done weekly many

of these cases healed admirably, and—to his surprise—there was great improvement in hearing, in comparison with that which resulted after the radical mastoid operation.

Sir James Dundas-Grant said that he had had a long experience with these cases. In the old days they took a long time to heal, and to become dry, and for adhesions to take place. He used Körner's flap, an incision along the upper pole, and one along the lower pole, the upper one cutting just into the cartilage. This was necessary in order to get sufficient opening, even if it left a little disfigurement of the meatus. The cartilage was dissected out and the thinned flap stitched back. He liked to use a very thin finger guard, like that used for rectal examination, but with a number of holes in it. This was inserted by means of Killian's long nasal speculum, afterwards being filled with a wick of gauze soaked with proflavin emulsion, which was a very good antiseptic. The finger-guard could be left in position several days. He did not stitch the posterior wound entirely, but left a little hiatus for drainage; there was then less chance of secretions detaching the plastic flap than if the wound was closed entirely. To diminish difficulty with the aditus, he chiselled away as much bone as possible. For any granulations he applied caustics, or, better still, a very fine galvano-cautery point.

He had had a striking case illustrating the difference in hearing power between a grafted and a non-grafted side. It was that of a middle-aged man who had marked trouble from suppuration. He (Sir James) operated on one side first, and at the end of a week he grafted it. The problem of the other side then arose, and when it was operated on the patient developed gouty phlebitis, so that grafting was out of the question. Both sides did very well, and the patient could hear sufficiently to enjoy life. Hearing on the grafted side, however, was better than on the other side. This was not unnatural, as there was not the same amount of cicatricial contraction.

The artificial drum was useful in post-radical-mastoid operation cases; in some the improvement of hearing was almost magical. He had had patients who had been hearing for twenty years with the help of nothing more than cotton-wool dipped in paraffin; in one case there was almost complete deafness without it.

With regard to the flap which was used by the President and Mr. Lake, he (the speaker) would fear that hair might grow on it. He referred to a case of cholesteatoma with very disabling vertigo, which he had grafted, but the graft was too thick. It began to discharge again, and there was renewed vertigo and cholesteatoma formation. He operated, turning out the posterior wall, but without finding anything remaining in the cavity. He found he had turned out the graft in the shape of the finger of a glove. He removed this completely and the vertigo disappeared entirely.

Mr. Sydney Scott said he considered that muscle-grafting was an advance. At St. Bartholomew's Hospital during the last thirty years there were relatively more radical than conservative mastoid operations in the earlier days than now. It was still necessary occasionally to perform the radical mastoid operation. He had elsewhere pointed out that the cutting of a flap was not an essential part of that operation.

He had used muscle-grafts for years, but only spasmodically, and when their use seemed to be specially indicated, so that he could not claim as great an experience as that of Mr. Kisch. An unmentioned occurrence was the occasional formation of a labyrinth fistula, following rapidly after a radical mastoid. At the time of the operation the eminentia arcuata externa was intact, and yet within three weeks or

so, labyrinth fistula symptom had developed. This had not been regarded as an indication for intervention, and when left alone, the fistula symptom had gradually disappeared. He could recall three such cases.

Mr. Forster had not mentioned the use of the wick drainage, he (Mr. Scott) was accustomed to use several strands of bipped cotton the size of No. 8 Chinese twist, the central strands of which could be withdrawn, the patient being scarcely aware of the procedure.

Mr. W. J. Harrison said that it was of great importance to keep the deeper parts of the cavity open in order to prevent the formation of granulations in that area. After the flap was fixed with a suture, it only needed light packing. The infection met with came, he thought, from the deeper parts of the canal where there was a tendency to narrowing. His practice was to pack firmly in the bottom of the cavity in order to prevent narrowing and the formation of granulations. Should any granulations form, they should at once be treated with silver nitrate or chromic acid, or by means of the cautery.

Mr. Bell Tawse said that the basis of his method of dealing with these cases was to leave the tympanum severely alone. He cut a flap merely to enable him to make an inspection of the cavity more easily, and for the same reason he inserted a small tube in the meatus, a much smaller one than Mr. Heath used. He did not put anything into the cavity, but irrigated it gently with normal saline for the first week. After that, the cavity was cleansed twice or thrice daily with sterile ribbon gauze or cotton-wool and an oily solution was applied. He did little operatively, except in his efforts to make access to the cavity adequate for the removal of granulations, and to render drainage as free as possible.

Mr. Ritchie Rodger said that in the discussion there had been common agreement that the middle ear should be respected as far as possible, and probably fewer radical operations were now performed. It was therefore all the more necessary to pay attention to something which had not been mentioned in the discussion, namely, the need for cleaning up the adjacent cavities. If a mastoid operation was performed—either radical or modified—while something was left at the other end of the eustachian tube which could prejudice the subsequent repair, a good result could not be expected.

Recently he had had the case of a young girl with acute mastoiditis; she had had a radical mastoid operation two months before on the other side, and that ear was still discharging, and blocked by granulations. In his examination he found one antrum dark, and the nasopharynx full of adenoids. He performed a Schwartze operation, and washed out the antrum, arranging to return in ten days to deal with the adenoids and to wash out the antrum again. On the second visit the antrum was still dirty, therefore, a week later, antral drainage was performed. By that time the ear operated on by himself was dry, with normal hearing, and in three weeks the other ear on which the radical operation had been done was nearly dry.

He made it a point to investigate the other end of the eustachian tube in every case, whether acute or chronic. Provided the case was not urgent, if there was anything in the nasopharynx or in the antrum or other sinuses, he tackled this while instituting conservative treatment of the ear, and often it dried up without the mastoid operation being required. If there was urgency, he performed the mastoid operation right away, and during the patient's three weeks in hospital he attended to any other cavities which required treatment.

Mr. Forster (in reply) said it had been difficult to decide at what point to begin a discussion on after-treatment, avoiding one on the performance of the radical mastoid operation, but he had been pleased to hear that some members favoured conservatism in operating for chronic middle-ear suppuration. He was grateful to Mr. Kisch for details and clear directions as to the use of the temporal muscle graft. He (Mr. Forster) had persuaded a colleague, only a few days before, to give this method a trial, for the closure of a post-aural fistula. He noted that Sir James Dundas-Grant liked to leave the lining of a cholesteatomatous cavity, and he thought that Dr. J. S. Fraser of Edinburgh agreed with Sir James on this point.

With regard to the use of a wick for draining the radical mastoid cavity, he himself had experience only of gauze, but he believed that worsted was advocated in Edinburgh. He had wondered whether, when bipp was used as a dressing in these cavities, bismuth granules might be left behind in the small bone spaces. Perhaps this was an unnecessary anxiety, though trouble had been reported from retention of granules after the simple mastoid or Schwartze operation.

He thanked Mr. Ritchie Rogers for emphasizing the importance of treatment of the nose and throat and of the accessory sinuses, though attention had usually been given to these parts before an operation upon the middle ear.

With regard to the lymphadenoid tissue of the pharynx, this of course raised a wide problem, but he was not so ready to blame this tissue for middle-ear disease as he had been in the past.

Section of Surgery

President—PHILIP TURNER, M.S.

[*January 2, 1935*]

Achalasia of the Cardia

By G. C. KNIGHT, F.R.C.S., and W. A. D. ADAMSON, F.R.C.S.

I. **Mr. G. C. Knight** : *The Innervation of the Œsophagus.*—An experimental investigation of the innervation of the œsophagus was undertaken, with the object of throwing light on the ætiology of achalasia of the cardia, or cardiospasm, and of determining whether or not it was feasible to treat this condition by sympathectomy.

At the present time many views are held as to the cause of the obstruction met with in this condition which postulate changes occurring either in structures adjacent to the œsophagus or in the œsophagus itself.

In the first group Mosher suggests that deformity of the liver tunnel may account for the obstruction, whilst Hill believes that incoördination of the relaxation of the diaphragm during deglutition is responsible, and Jackson postulates an actual phrenospasm. In the second group, Shaw and Woo state that kinking of the œsophagus is responsible, but Hurst and Walton believe that the fault lies in a derangement of the nervous control of the cardia, Hurst maintaining that there is paralysis of the normal opening mechanism, while Walton affirms that there is no paralysis but rather spasm of the part, presumably due to sympathetic overaction.

For either of these views to be effective there must exist at the cardia a true intrinsic sphincter which is modified in tonus by the action of extrinsic nerves. A survey of the experimental results on this subject shows a great lack of uniformity in the results obtained, most probably due to the variety of experimental animals employed. The investigation was therefore carried out on cats, the structure of the œsophagus in these animals corresponding most closely to the human.

By stimulation experiments it was shown that there is a true intrinsic sphincter at the cardia which is relaxed by the vagus and contracts on sympathetic stimulation. The sphincter is capable of functioning independently of surrounding structures, and receives its sympathetic supply from the cœliac plexus in fibres which follow the course of the left gastric artery and its œsophageal branch to the lower end of the œsophagus.

Excision of the extrinsic nerves supplying the œsophagus, as studied by skiagrams taken of bismuth meals, showed that vagal excision reproduced the X-ray pathological and clinical picture of achalasia of the cardia, the sphincter failing to relax in the

course of peristalsis. If, however, both thoracic sympathetic chains were excised at the same time as the vagi were divided, no obstruction resulted at the cardia. The activity of the sympathetic is therefore essential for the obstruction to occur. Denervation by the operation of cœliac sympathectomy of the sympathetic fibres described above as supplying the cardiac sphincters, resulted in a complete loss of sphincter tonus so that the meal could be caused to regurgitate from stomach to œsophagus. Later, the tonus recovered somewhat, but there was abnormally rapid passage of the meal through from œsophagus to stomach.

In animals in which achalasia of the cardia had been produced by vagal section, subsequent cœliac sympathectomy resulted in a complete relief of symptoms, and skiagrams showed the sphincter relaxing and the meal entering the stomach without obstruction. The success of sympathectomy is to be judged on this relaxation of the sphincter, rather than on regurgitation from stomach to œsophagus, which disappears as the muscle recovers tonus after the operation.

A criticism of these results is that the vagal lesion caused experimentally did not affect the intrinsic neuromuscular mechanism of the œsophagus. In man it may be that the lesions of Auerbach's plexus, described by Rake, might interfere with the recovery of the tonus and peristalsis in the œsophagus. If this be so, one would expect greater benefit to be derived from the operation in cases of a spasmodic type with a normal œsophagus, than in cases in which Auerbach's plexus was involved, as the latter would still lack peristalsis despite diminished sphincter tonus.

II. **Mr. W. A. D. Adamson** : *Sympathectomy for Achalasia of the Cardia.*—Mr. Knight has shown clearly the experimental evidence in favour of cardiospasm being of neurogenic origin and it only remained to try out his work on the human subject.

The operative procedure has been designed to interrupt the sympathetic nerves supplying the lower end of the œsophagus. With the patient lying on a gall-
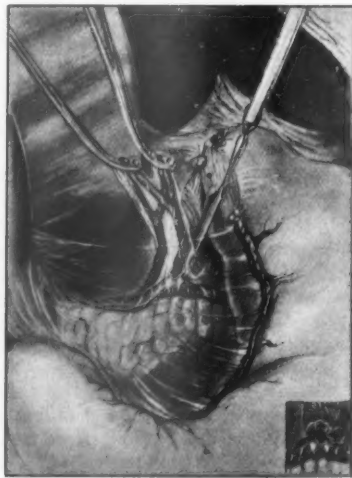

FIG. 1.　　　　　　　　　　FIG. 2.

FIGS. 1 and 2.—The left gastric (coronary) artery and its œsophageal branch have been divided. Dissection is being carried down to the cœliac artery.

bladder cushion, a left paramedial incision is made, extending upwards as far as the xiphisternum and downwards to the level of the umbilicus. It was thoughtthat the left lobe of the liver would require to be mobilized but this has never been found necessary. The left gastric (coronary) artery is exposed high up on the lesser curvature of the stomach (fig. 1). It is freed and ligatured, along with its vein, the ligature containing a mass of tissue that will be found lying around it (fig. 1). With artery-forceps on the central end of the vessels acting as a retractor, a downward pull is exerted and the œsophageal branch of the artery made to stand out. This is dissected free and on its right side a bundle of nerve tissue will be constantly found. The œsophageal branch of the artery, along with this bundle of nerve tissue, is ligated and pulled with artery forceps over to the patient's right (fig. 2). In this way the deep aspect of the left gastric artery is exposed, and here many strands of nerve tissue will be found passing from the cœliac axis to the lower end of the œsophagus. These are all divided at their peripheral ends. Dissection is then carried centrally until the left side of the cœliac axis is exposed. The last stage of the operation is to ligate the left gastric artery at its origin from the cœliac and so to remove the segment of the artery along with the mass of nerve tissue that has been dissected free (fig. 2, inset). On section this mass of tissue has been found in each case tobe composed of numerous bundles of non-myelinated nerve-fibres. The abdomen is closed in the usual way.

This operation has now been carried out with slight modifications in four cases.

Case 1.—H. F., aged 27, butcher, on November 25, 1933, developed a perforated duodenal ulcer. He was operated on about six hours later and a simple closure of the perforation was carried out. He had a very stormy convalescence. He developed a cough and burst the wound. This was closed and eventually he was discharged from hospital on January 9, 1934, with a ventral hernia.

He was readmitted to the ward on May 12 with a complaint of vomiting after food. X-ray examination showed a markedly dilated œsophagus with an apparent narrowing situated some little distance above the diaphragm. The patient stated that the vomiting had first appeared about three weeks after his discharge from hospital.

The œsophagoscope was passed at this time and it was noted that the upper part of the œsophagus was markedly dilated with a spasm of the lower end. Œsophageal bougies were passed and the patient was discharged on May 21 very much improved. He was readmitted on July 27, 1934, with a recurrence of the vomiting. X-ray examination again showed considerable dilatation of the œsophagus (fig. 3). A mercurial bougie was passed and he obtained relief for four days.

The operation of lower œsophageal sympathectomy was performed on August 14, 1934. The patient made a very satisfactory recovery. He had no further difficulty in swallowing. His weight on leaving hospital three weeks after the operation was 8 st. 11 lb. He has continued up to date with no further difficulty in swallowing (fig. 4, p. 30) and is able to eat any food. His weight now is 10 st. 6 lb.

Case 2.—R. R., aged 45, slater, stated that he had had difficulty in swallowing, of two years' duration. The onset followed the extraction of his teeth. He has had two good sets of dentures which he wears continuously. Since the onset of symptoms he has lost 2 st. in weight. The difficulty in swallowing has occurred in attacks, so that every two or three weeks he has a bout of difficulty in swallowing associated with regurgitation of undigested food which will last for several days. The attack would then gradually subside, and he would be fit for another two or three weeks. X-ray examination showed some dilatation of the œsophagus (fig. 5). The œsophagoscope showed the dilatation of the œsophagus with a contraction, which appeared to be of spasmodic nature, of the lower end.

The operation of lower œsophageal sympathectomy was performed on October 19, 1934.

During the first fortnight after operation the patient appeared to be completely cured. He was able to take the ordinary hospital light diet without difficulty. He then had recurrence of his symptoms with a considerable amount of vomiting, the vomited material being alkaline

FIG. 3. *Case 1.* FIG. 4.

FIG. 3.—Skiagram taken before operation, half an hour after swallowing barium.

FIG. 4.—Skiagram taken four months after operation. This plate was taken half a minute after swallowing barium. It shows the reduction in size and also the passage of the barium into stomach.

in reaction and consisting of unaltered food. At the end of a further fortnight the symptoms were still present, and accordingly a mercurial bougie was passed. This gave immediate relief, and on reporting on December 20, he stated that he had had no further recurrence of his symptoms, that he was able to take any food, and had gained a stone in weight. A skiagram taken on this date still showed a considerable amount of dilatation of the œsophagus, but the barium was now seen to pass through the lower end into the stomach (fig. 6).

Case 3.—R. S., aged 28, boot repairer, in April 1934 developed pneumonia and two days later, after a meal, he vomited. For a fortnight he had difficulty in swallowing, associated with vomiting, and then this symptom gradually diminished. At this time an effusion developed into the left side of his chest which required to be tapped. A month after the first onset of the symptoms they began to recur, and he has continued to vomit usually once a day from that time up till his admission to hospital. The food came up suddenly ; it was not sour to the taste, and it seemed to consist of the food that he had eaten, mixed with frothy material. Some difficulty was found in obtaining a satisfactory skiagram of the œsophagus as it was always filled with food. It was washed out, about half a pint of pultaceous material being

FIG. 5.   *Case 2.*   FIG. 6.

FIG. 5.—Skiagram taken before operation, half an hour after drinking barium.

FIG. 6.—Skiagram taken six weeks after operation. Barium is seen entering the stomach but there is no diminution in the size of the œsophagus.

removed. After this a very satisfactory skiagram was obtained (fig. 7). In this case it was thought that as there had been a toxic illness, he might have developed a toxic neuritis of the vagus nerve which would have accounted for the increase of tonus of the lower end of the œsophagus. In addition, however, such a lesion would produce a relative increase of the inhibitory fibres to the upper part of the œsophagus, and it was therefore thought that this patient's difficulty in swallowing may have been due as much to a partial paralysis of the upper part of the œsophagus as to an insufficient relaxation of the lower end. Accordingly both stellate ganglia were anæsthetized with one-per-cent. novocain, a Horner's syndrome being produced, first on the one side and then on the other. The patient was screened as soon as it was evident that both stellate ganglia were paralysed, but no alteration in the appearances of the œsophagus was seen.

The operation of lower œsophageal sympathectomy was performed on November 12, 1934. The œsophagus was washed out an hour before operation. The operation in this case was somewhat more extensive and a block dissection was made of all the tissues lying between the lower end of the œsophagus and the uppermost part of the lesser curvature of the stomach across to the left side of the aorta. The patient was considerably upset by the operation. His abdomen became distended, his pulse-rate went up to 140 and it was feared that the worst might happen. He gradually improved, however, and eventually made a very

satisfactory recovery. His weight previous to the onset of the pneumonia was 9 st. 9 lb. His weight on admission to hospital for treatment of the cardiospasm was 8 st. 8 lb. His weight on December 20 was 10 st. He now eats an ordinary diet but during the last fortnight he has had one attack of vomiting. On December 20 no difficulty was experienced in obtaining a very satisfactory skiagram even although he had had a meal as recently as two hours before the examination, thus showing that there is now no collection of food in the œsophagus (fig. 8).
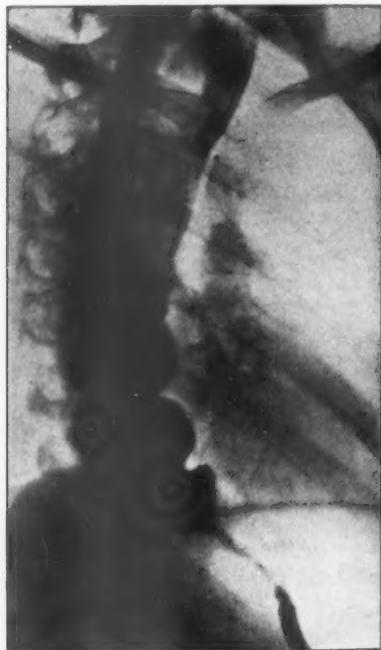
FIG. 7.   *Case 3.*   FIG. 8.

FIG. 7.—Skiagram taken before operation, half an hour after taking barium.

FIG. 8.—Skiagram taken six weeks after operation. Plate taken two minutes after swallowing barium. No alteration in size of œsophagus, but barium seen entering stomach.

Case 4.—A. M. C., aged 29, for nine years has experienced difficulty in swallowing. During the past seven years he has passed an œsophageal bougie every other day. If he failed to pass the bougie he always had difficulty in swallowing. He would on occasions pass the bougie more frequently than this, notably before going out to dinner. X-ray examination of the œsophagus before operation showed a little dilatation but the barium took a long time to pass through into the stomach.

The operation of lower œsophageal sympathectomy was performed on December 11, 1934. The usual operation was carried out. The patient made a satisfactory recovery. He has not passed a bougie since. During his stay in the nursing home his symptoms were com-

pletely relieved. Since returning home he has on two occasions had some difficulty in swallowing.

Summary.—Operative procedure has been carried out in four cases. In the earliest case—in which five months have elapsed since the operation—there has been complete cure so far as the patient's symptoms are concerned. There is still some dilatation of the œsophagus but the barium on screen examination is seen to pass into the stomach quite easily. The other three cases show improvement in symptoms although radiologically there is no difference in the size of the œsophagus but only in the rapidity with which the barium enters the stomach.

It is too early to draw any conclusions from these cases but they are sufficiently encouraging to warrant a further trial of the operative procedure.

I have to acknowledge my indebtedness to Mr. J. W. Struthers, Mr. J. M. M. Graham and Professor D. P. D. Wilkie for permission to publish the case reports.

Sympathectomy for Achalasia of the Cardia.—Case reported by G. C. KNIGHT, F.R.C.S.

One patient has been operated on at St. Bartholomew's Hospital by Professor G. Gask.

She was a woman, aged 48, with seven years' history of dysphagia and vomiting which had persisted despite five years' treatment with œsophageal bougies.

A double subcostal incision was employed, with transverse division of the muscles. The left lobe of the liver was mobilized, and the left gastric artery was excised from its origin to its œsophageal branch, together with a large number of adjacent nerve trunks. At operation the sphincter was felt to be enormously thickened, approximately one inch and a half in length and the size of a man's thumb.

After operation the patient's symptoms were much relieved, but X-ray examination six weeks later still showed some delay at the cardia.

This is of interest, as cases showing this muscular hypertrophy differ from the usual type of achalasia or cardiospasm in that the obstruction persists after death, whereas in the latter there is no muscular hypertrophy and no obstruction can be found at post-mortem examination. It would appear, therefore, that less benefit is to be expected from neurectomy in these extremely rare cases of hypertrophic stenosis of the cardia which simulate exactly the symptoms and X-ray appearances of achalasia.

Chronic Staphylococcal Osteomyelitis of the Spine

By CECIL FLEMMING, F.R.C.S.

IT is the purpose of this communication to place on record the reports of five cases of chronic osteomyelitis of the spine which seem to belong to a definite clinical type. The condition has been previously described and some references of the published accounts are given at the end of this paper. It is, however, desirable that as many cases as possible should be recorded, so that the clinical type may become more widely known and more easily recognized, for, to judge from our own experience and that of others, these cases are liable to be diagnosed as cases of tuberculous infection and the patients, in consequence, may undergo a course of treatment which is unnecessarily tedious.

Case 1.—A man, aged 40, in November 1930, developed a boil on the forearm which did not heal for three months. Then he became ill, with generalized pains, headache, etc., and was in bed for three weeks. On getting up he noticed pain in the middle of the back. One month later he noticed a tender swelling on the right shin.

On examination.—Tender over 7th and 8th dorsal spines : slight rigidity : no abscess found : skiagram showed diminution of joint-space between the bodies of the 7th and 8th dorsal vertebræ with irregularity of bone. Diagnosed from the skiagram as tuberculous infection. Skiagram of tibia showed a chronic abscess in the bone which was opened and contained pus and *Staphylococcus aureus.* Spinal infection assumed to be the same.

Treatment.—Fixation in plaster for three months, ambulatory after first week.

Present condition.—He has had no symptoms for the last four years. X-ray examination shows fusion between the bodies of the 7th and 8th dorsal bodies.

Case 2.—A man, aged 47, in June 1933, began to have occasional pain in the back, which became gradually worse during the next six months. In the same month as the pain in the back began, he had a boil on the face and in the following month another boil appeared but there was no general illness. A skiagram (fig. 1) shows apparent fusion between the bodies

FIG. 1.—*Case 2.* Showing apparent fusion between the bodies of the 10th and 11th dorsal vertebræ, without collapse.

FIG. 2a.   *Case 4.*   FIG. 2b.
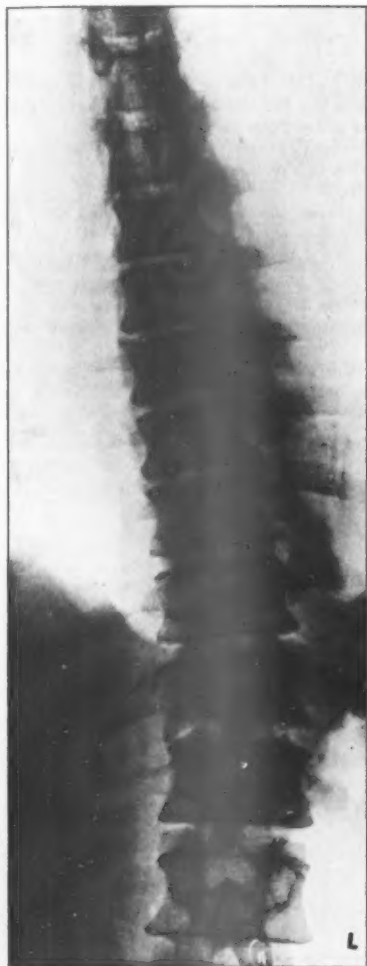
FIG. 2a.—Slight irregularity of the adjacent parts of the bodies of the 12th dorsal and 1st lumbar vertebræ. Diagnosed as tuberculosis.

FIG. 2b.—Same case twelve months later, after Albee operation had been performed. Partial disappearance of joint-space. In the lateral view there was no collapse of the bodies of either vertebra. Simultaneous chronic abscess of ischium.

of the 10th and 11th dorsal vertebræ. No apparent destruction of bone in this case. Treated by fixation in plaster for three months. Considerable, but not complete, relief of symptoms.

Case 3.—A man, aged 54, in April 1932, had a carbuncle on the buttock from which he made a fairly rapid recovery. Two months later he fell ill and went to bed for a few days: there were no definite symptoms. On getting up he noticed a pain in the lower part of the back, and had spasms of pain in both legs.

On examination.—There was an angular deformity at the level of the 1st lumbar vertebra. A skiagram showed partial collapse of the bodies of the 1st and 2nd lumbar vertebræ, and in addition shadows suggesting new bone-formation around the bodies. No signs of pressure on the cauda equina, despite the symptoms. Diagnosis of staphylococcal infection made on the history, and the suggestion of new bone-formation in the skiagram.

Treatment.—Fixation in plaster for three months.

Present condition (after two years).—He has pain in the back on stooping; otherwise he is quite well.

Case 4.—A man, aged 53, in April 1931, had a boil on the neck. One week later fell ill and was in bed for three months with fever and general symptoms. A month after the onset of this illness he had some pain in the back. The pain was not severe and after he got up from bed was only occasional for the next two months: it then suddenly became worse, compelling him to return to bed.

On examination.—There was tenderness over the 12th dorsal spine and slight rigidity. A skiagram (fig. 2a) showed narrowing of the space between the 12th dorsal and 1st lumbar vertebræ, with a little rarefaction of the bone of each.

FIG. 3.—*Case 5.* Irregularity of adjacent parts of bodies of 3rd and 4th cervical vertebræ. Lesion healed after fixation for ten weeks only.

Despite the history and the recollection of the other cases, the radiographic appearances were thought to be so like those of a tuberculous infection that a bone-grafting operation was performed and the subsequent treatment was based on the assumption that the case was one of tuberculosis.

One year after the patient left hospital, he began to complain of pain in the left hip region. A skiagram taken of the pelvis showed an abscess of the ischium. The central area of rarefaction and the surrounding ring of increased density of the bone were exactly like the appearance of a chronic staphylococcal abscess. Fig. 2*b* is a skiagram of the spine, taken at this time.

The abscess has not as yet been opened. Assuming that the infection of the ischium is staphylococcal it seems reasonable to suppose that the spinal infection was of the same nature. The whole history of the case is very similar to that of the first case reported in this paper.

Case 5.—A man, aged 55, in February 1934, had a kidney removed on account of a staphylococcal infection. One month later he began to have shooting pain on the left side of the neck and in the left shoulder. A skiagram of the cervical spine (fig. 3) shows destruction of the adjacent parts of the bodies of the 3rd and 4th cervical vertebræ. The appearance could be explained on the assumption of a tuberculous infection, but in view of the primary infection of the kidney with the staphylococcus, the vertebral infection was diagnosed as being of the same type. The spine was fixed in plaster for ten weeks. After removal of the plaster there was no recurrence of symptoms.

Commentary

In these case records a large number of detailed observations have been deliberately omitted in order that more emphasis may be laid on the important and distinguishing features.

The negative points common to all these five cases may be noted first. In none was there any abscess detected which might have arisen from the vertebræ: in none was there any direct proof that the infection was staphylococcal. None of the patients when seen were very ill, though three had slight fever and a slight increase in pulse-rate. The absence of these features differentiates these cases from the well-recognized cases of acute staphylococcal osteomyelitis of the spine, and here two questions are raised. Firstly, do the cases now reported prove the existence of a definite clinical type of chronic staphylococcal osteomyelitis? Secondly, if so, how is this condition to be differentiated from tuberculosis of the spine?

A study of the skiagrams (not all of which are illustrated in this paper) shows that in the early stages there is a diminution in the intervertebral space and slight irregularity of the edges of the adjacent bodies. The picture at this stage is indistinguishable from that of a tuberculous infection. Later the two adjoining bodies come into contact and fuse, possibly with some collapse of the bodies but usually the shape of the bodies remains fairly regular. There may be shadows suggesting the formation of new bone at the sides of the bodies. At this stage the resemblance to the radiological picture of tuberculosis is less close. The difference is the more evident if the case has been under observation from the first, for the whole process of irregularity of the intervertebral space, disappearance of the space, and fusion of the bodies, takes place within a period of three months. So rapid a rate of healing is extremely improbable in a tuberculous lesion. The nature and the rapidity of the healing process are of themselves suggestive of a staphylococcal infection. Additional evidence is to be found in two of the cases. In Case 1 there was a simultaneous proven staphylococcal abscess of the tibia. In Case 4 there was a subsequent chronic abscess of the ischium which had the appearance of being staphylococcal in origin.

The existence of a second staphylococcal lesion elsewhere cannot be expected in every case and it is desirable to be able to make the diagnosis correctly in the early stages of the disease at a time when the radiological appearances are often very like those of a tuberculous infection. The history of the cases reported here in each instance gives a lead to the diagnosis. The features which are important are: a primary staphylococcal lesion, in four cases situated in the skin, followed by an illness without specific character, followed in turn by pain in the back. The time-relations of the appearance of these symptoms is variable, and in the second case reported there was no illness sufficiently severe to confine the patient to bed.

A history of this type should lead, at least, to a consideration of the possibility that the spinal infection is staphylococcal and not tuberculous. If the former is diagnosed, fixation for three months in plaster, the patient not being confined to bed, is adequate to allow the lesion to heal. If the patient is treated on the basis that tuberculosis is the cause of the spinal disease, the treatment will naturally be suitable for a staphylococcal infection, but should there be radiological evidence of an unduly rapid rate of healing of the spine, it would appear reasonable to reconsider the diagnosis in favour of a staphylococcal infection and to release the patient from treatment at the end of three months.

REFERENCES

DE FOREST SMITH, A., *Journ. Am. Med. Ass.*, 1933, ci, 335.
STEINDLER, A., "Diseases and Deformities of the Spine," Lond., 1929.
OEHLECKER, F., *Beitr. z. Klin. Chir.*, 1935, cxxxiv, 1.

Acute Osteomyelitis of Atlas and Axis, with Recovery.—T. HENRY WILSON, F.R.C.S.

A police inspector, aged 43, was admitted to hospital in October 1933, complaining of frequency of micturition, hæmaturia and severe pains at the back of his neck.

Previous history.—He had gonorrhœa in 1910, but reactions to tests in 1929 were all negative. Had rheumatic fever when aged 15 and malaria during the war in East Africa.

Present history.—In February 1933, he had an attack of " influenza," followed by pain in the left hip and difficulty in walking; a peri-anal abscess was opened in May 1933, after which the hip returned to normal. A series of carbuncles followed. He had a further attack of " influenza " five weeks before admission; sudden onset of severe pains in the neck accompanied by a series of swellings on the scalp, which cleared within twenty-four hours, three weeks before admission; and one week of scalding micturition, hæmaturia and frequency.

State on admission.—Temperature 97·4, pulse 90, respirations 16. He moved his head as little as possible on account of pain and had partial rotation to the left only; there was an area of marked tenderness over about the third cervical spinous process; a clear urethral discharge containing a few pus-cells and extracellular cocci; the urine contained blood and pus-cells in quantity. A skiagram of the urogenital tract showed no calculi and that of the neck appeared normal.

Progress.—A further investigation did not reveal any residual gonococcal infection and the blood Wassermann and complement-deviation reactions were negative; there was a leucocytosis of 11,600 cells, of which 72% were polymorphonuclears.

On November 18 the temperature rose to 99·4, and the pulse to 116; the pain in the neck was worse and a skiagram (fig. 1) showed dislocation of the atlas forward on the axis; he was kept lying still in bed, but on November 28, 1934, the temperature rose to 102, the neck appeared to become collapsed and broadened, and the posterior pharyngeal wall became œdematous. A further skiagram showed the dislocation to have increased. There were never any abnormal signs in the central nervous system.

FIG. 1.—Skiagram taken November 18, 1933, before treatment of neck was begun.

FIG. 2.—Skiagram taken January 27, 1934, showing consolidation.

He was now treated with a weight-extension of 5 lb. under the chin, and marked improvement resulted with regard to the pain.   By this time the urinary signs had all cleared up and the urine was sterile on culture.   A skiagram taken fourteen days after the traction had been applied showed that the deformity was reduced. In December the temperature fell to normal and remained there.   The extension was removed on April 11, 1934, and a moulded leather neck-support was fitted.   Before this a skiagram, taken on January 27, 1934, showed the bones in good position relative to each other and fusion commencing (fig. 2).   The patient was allowed out of bed on May 26 and discharged from the ward on June 29, 1934.

Since that time he has been kept under observation and is in good health ; he still wears his neck-support when out-of-doors.

Section of Urology

President—J. B. MACALPINE, F.R.C.S.

[February 28, 1935]

The Prognosis of Malignant Renal Tumours

By E. G. MUIR, M.S., and A. J. B. GOLDSMITH, F.R.C.S.

MALIGNANT tumours of the kidney have for years been a subject of interest to pathologist and surgeon. To the former, in the possible origin of the various types of tumour; to the latter, in their diagnosis and treatment. It is perhaps true to say that pathological enthusiasm is on the wane, since there is now some unanimity of opinion, at any rate in decrying the arguments once put forward with enthusiasm by Grawitz [1]. New and improved methods have rendered diagnosis easier for the surgeon.

There is a third standpoint—that of the patient. To him prognosis must take first place, and criticism can justly be levelled against the surgeon who, before performing an operation with a definite mortality, does not first consider the ultimate prognosis and then acquaint the patient, if not with the whole unpalatable truth, at least with some measure of it.

In 1909, Garceau [2] of New Orleans published his book on "Tumours of the Kidney" and his findings have frequently been quoted by other writers. He collected 176 cases of renal tumour, in 143 of which nephrectomy was performed with an operative mortality of 23% [Table I].

TABLE I.—TUMOURS OF THE KIDNEY (GARCEAU)

176 cases (All types). 143 nephrectomies. Operative mortality 23%

Post-operative Results :—

Dead 43 (77% of deaths proved due to recurrence)

0-1 year	22 cases		4-5 years	1 case
1-2 years	11 ,,		7-8 ,,	1 ,,
2-3 ,,	6 ,,		10-11 ,,	1 ,,
3-4 ,,	1 case			

Survivals 31

0-1 year	9 cases		4-5 years	3 cases
1-2 years	6 ,,		5-6 ,,	2 ,,
2-3 ,,	7 ,,		6-7 ,,	1 case
3-4 ,,	2 ,,		9-10 ,,	1 ,,

Result not stated 36 cases

3-year survival rate of 74 cases submitted to nephrectomy (13) = 19%

Thompson-Walker [3] summarizes Garceau's findings by stating that the average duration of life after the appearance of the first symptom is three and a half years and that with operative treatment only 7 to 10% survive to the end of the fourth

year. One might go further and point out that of 143 cases subjected to nephrectomy Garceau was only able to find two patients alive after ten years and one of these died from recurrence before the eleventh year.

In children recurrence is stated to be more rapid and there is a higher operative mortality.

In a recent clinico-pathological survey of hypernephromata, Gottesman, Perla and Elson [4] found that malignancy was very variable. In 30% of their cases the tumour was a chance observation at autopsy. They concluded that the neoplasm might exist for many years before the onset of symptoms and that there was a marked variation in the rate of growth and in the interval between the onset of symptoms and the death of the patient.

When we examine the details of their clinical cases, however, this appears to be perhaps a somewhat optimistic conclusion, for out of 28 cases in which the diagnosis was made clinically, 15 were already inoperable from the presence of secondaries, and in the 13 cases of nephrectomy the average duration of life was only two years, the longest being seven years.

Slightly more encouraging results have been reported by Swan [5]. Out of 51 cases of renal carcinoma, nephrectomy was possible in 32, with an operative mortality of 16% (five cases). Of these 32 patients, 13 were alive or had died without recurrence at the time the article was published. It will be seen from the accompanying table that eight out of 32 patients (25%) were alive after three years, the longest survival being just less than twelve years. The results of five nephrectomies for renal sarcoma are also shown.

TABLE II.—TUMOURS OF THE KIDNEY (SWAN).

CARCINOMA OF THE KIDNEY.　51 cases.　32 nephrectomies.　Mortality 16%.

13 cases alive or died without recurrence.

0-2 years	4 cases	...	8-9 years	2 cases
2-3 ,,	1 case	...	9-10 ,,	1 case
5-6 ,,	2 cases	...	11-12 ,,	1 ,,
6-7 ,,	2 ,,			

8 out of 32 patients alive after 3 years = 25%.

SARCOMA OF KIDNEY.　8 cases.　5 nephrectomies.　Mortality nil.

Dead.			*Alive.*	
0-1 year	2 cases	...	1-2 years	1 case
			2-3 ,,	1 ,,

1 case untraced.

At the International Congress of Urology in 1933 Swift Joly [6] collected a large number of cases of malignant epithelial tumours of the renal pelvis. Out of 125 traced cases of nephrectomy for this condition 27% (34 patients) were alive at varying periods up to and including five years ; 5% (six patients) were alive over five years after nephrectomy. These results are not encouraging and suggest that there is little difference in prognosis between malignant tumours of the renal pelvis and those of the kidney itself.

We have collected 29 cases of malignant renal tumour in all of which nephrectomy was performed, with a view to considering what factors, if any, influence the prognosis in these unfortunate patients.

The first factor is the histology of the tumour.

Histology.—We have divided these tumours into four groups: hypernephroma, granular-celled papillary carcinoma, carcinoma of the renal pelvis and mixed tumours.

The microscopical appearances of a hypernephroma are too well known to merit description.

A granular-celled papillary carcinoma is a tumour with coarsely granular cells and a well-marked papillary arrangement. Occasionally in these cases there are

multiple primary growths in the kidney. They closely resemble and may have a developmental relationship with the small subcapsular papillary adenomata which are found not uncommonly in kidneys at routine post-mortem examinations.

Carcinoma of the renal pelvis and mixed renal tumours require no description. The following table gives details of the survival periods in the various groups.

TABLE III.—TUMOURS OF THE KIDNEY (Present Series)

HYPERNEPHROMA : 10 nephrectomies. Operative deaths 2

Died from recurrence	*Alive*
0-1 year 1 case	0-1 year 1 case
1-2 years 1 ,,	2-3 years 1 ,,
7-8 ., 1 ,,	7-8 ,, 1 ,,
	11-12 ,, 1 ,,

1 case untraced.
3-year survival rate of 10 cases submitted to nephrectomy (3) = 33%.

GRANULAR-CELLED PAPILLARY CARCINOMA : 13 nephrectomies. Operative deaths 1

Died from recurrence	*Alive*
0-1 year 7 cases	0-1 year 2 cases
1-2 years 1 case	3-4 years 1 case
15-16 ,, 1 ,,	

3-year survival-rate of 13 cases submitted to nephrectomy = 15%.

CARCINOMA OF PELVIS. 5 nephrectomies. Operative deaths, nil

Died from recurrence	*Alive*
0-1 year 2 cases	2-3 years 1 case
1-2 years 2 ,,	

SARCOMA OF KIDNEY. 1 nephrectomy. Operative deaths, nil
Died in less than 1 year from recurrence.

In such a small number of cases it is difficult to draw any conclusions. In the two largest groups it is interesting to note that the percentage of 3-year cures in the hypernephromata is 33% and 15% in the granular-celled papillary carcinomata. In the latter group many of the patients died within the first year.

One patient with a granular-celled papillary carcinoma survived over fifteen years, only to die of recurrence. She was a woman aged 42 and was admitted to the Middlesex Hospital in August 1916, when nephrectomy was performed on account of an encapsulated tumour in the lower pole of the left kidney. Convalescence was uneventful, and her subsequent health was satisfactory until 1931, when she complained of pain in the back and left loin. An irregular mass was then present in the left hypochondriac region, and a few months later a skiagram showed a secondary deposit in the neck of the left femur. The patient died in April 1932, fifteen years and eight months after the nephrectomy. At post-mortem examination a mass of growth was found in the loin, adherent to the spine and spreading down towards the pelvis. The liver was greatly enlarged by many secondary deposits, and secondary deposits were also present in the pelvic peritoneum. The right kidney was somewhat enlarged but otherwise normal. This case is unique in the length of time which elapsed between operation and recurrence.

We attempted to make some classification of these tumours by Broder's method, but abandoned it owing to the difficulty in comparing one type of growth with another. If one can draw any conclusion from a histological classification, it is that recurrence appears to take place more rapidly and more certainly in the granular-celled papillary carcinomata than in the hypernephromata.

Size and extent of the tumours.—Apart from the general condition of the patient, the factors which increase the difficulty of the operation and its mortality are the size of the tumour and the presence of many adhesions.

In 14 cases in this series it was noted at nephrectomy that the growth had involved the perinephric tissues or the pedicle of the kidney and the renal vein, or that enlarged glands were present. One of these patients died following the operation; two were untraced; of the 11 remaining patients all died from recurrence, nine of them within one year. The average duration of life after nephrectomy was only eight months. The average duration of life for all cases in this series was two years and nine months, including eight patients still alive and free from recurrence.

These figures only bear out the obvious—that the surgeon who removes an advanced malignant renal tumour can be certain that the patient has but a few months to live.

Does the converse hold true? Can a relatively good prognosis be given when the tumour is small or almost encapsulated.

In nine cases in this series the growth was early or encapsulated. Their average duration of life was four years two months, including three patients still alive and free from recurrence. It is natural that we should expect a somewhat better prognosis. Unfortunately, it is in these small renal tumours that occasionally the first symptom of disease is the appearance of a distant metastasis.

Type of operation.—Thompson-Walker [3] has stated that the ideal operation should remove the kidney and growth, the adipose capsule, lymph vessels and glands, and the fat in which they are embedded and the suprarenal glands. A similar view was stated by Garceau [2].

In many of the cases in this series a certain amount of perirenal fat was removed with the kidney, but in few, if any, was the suprarenal gland or the adjacent lymph glands removed. Yet the figures in this series of the survival period do not appear to be worse than those given by other writers, and the immediate operation mortality of 10% is somewhat better.

With the ultimate prognosis grave, and the operative mortality considerable, it appears doubtful whether anything should be added to the operation of simple nephrectomy, or even if this should be persisted in when exploration has shown the diagnosis to be certain, the kidney adherent, and the operation a difficult one. This operation should never be regarded as of the " kill or cure " variety.

X-ray therapy.—Only a small number of these cases have been treated by X-ray therapy and then usually after local recurrence had taken place.

Two patients were given post-operative prophylactic X-rays. One of these is alive and free from recurrence two years later : the other, a patient with a large and adherent renal growth, died within a year.

We are obviously unable to come to any conclusions as to the value of this treatment, but it is felt that any treatment which might possibly benefit the patient should be tried.

TABLE IV.—TUMOURS OF KIDNEY (Present Series)

37 cases (All types). 29 nephrectomies. Operative mortality (3) 10%

Post-operative Results :—

Dead 17 (95% of deaths due to recurrence)

0-1 year	11 cases		7-8 years	1 case
1-2 years	4 ,,		15-16 ,,	1 ,,

Survivals 8

0-1 year	3 cases		5-6 years	1 case
2-3 years	2 ,,		11-12 ,,	1 ,,
3-4 ,,	1 case			

1 case untraced

3-year survival rate.	5 cases, 20%
5 ,, ,, ,,	4 ,, 16%
10 ,, ,, ,,	2 ,, 8%
15 ,, ,, ,,	1 case 4%

Conclusion.—This last table includes all cases in this series and indicates the high mortality of this disease. No patient, known to be alive and well, has yet lived as long as the patient who died of recurrence nearly sixteen years after nephrectomy.

One is tempted to ask if a patient can ever be considered cured. Garceau [2] stated that "An individual who has had nephrectomy performed for removal of the diseased organ, even if the operation has been an early and a thorough one, is never to be considered safe from the danger of a recurrence. . . ."

At the present time there is no remedy other than surgery which can be offered to the patient. A successful nephrectomy may prolong life for many years—even though there is only a faint chance of permanent cure—and the exploration sometimes enables the diagnosis to be made.

Nor does Fortune never smile on surgical endeavour. A solid renal tumour weighing 22 lb. was removed from a woman aged 20 by Gordon-Taylor [7]. She made an uninterrupted recovery and histological examination showed the growth to be innocent—an adenofibroma of the kidney. Here, perhaps where least expected, an excellent prognosis could be given. The patient was alive and well eight years later, and is the mother of three children.[1]

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REFERENCES

1 GRAWITZ, *Virchow's Arch.*, 1883, xciii, 39.
2 GARCEAU, "Tumours of the kidney," 1909.
3 THOMPSON-WALKER, J., Choyce's "System of surgery," 1925, ii.
4 GOTTESMAN, J., PERLA, D., and ELSON, J., *Archiv Surg.*, 1932, xxiv, 722-751.
5 SWAN, R. H. JOCELYN, *Brit. Med. Journ.*, 1933 (i), 606-610.
6 JOLY, J. SWIFT, *Trans. Fifth Cong. Internat. Soc. Urol.*, 1933, i, 211.
7 GORDON-TAYLOR, G., " The dramatic in surgery," 1930.

Some Points in the Diagnosis of Stone by X-rays

By C. A. WELLS, F.R.C.S.

ABSTRACT.—The investigation of cases suspected of stone is concerned with (1) those in which a shadow is visible and (2) those in which X-rays throw no shadow.

In the former group the nature of the shadow must be determined. If a stone, it must be accurately placed in the urinary tract and the anatomy and function of the affected and unaffected parts of the tract must be determined.

A stone may be recognized by the characteristic shape to which it grows in the pelvis, in a calyx or in the ureter. In the earlier stages, or when the shape of the shadow is not characteristic, radiograms may be made on inspiration and expiration. In orthopædic and other cases immobilized for long periods interesting calculi may form and may subsequently be disintegrated and passed, or may require surgical treatment.

For stones in the kidney and upper ureter pyelography by the descending route is ideal. For infected stones the retrograde route is preferable. For small ureteric stones an opaque catheter is best.

Non-opaque stones are of real surgical significance. It is essential to make a positive diagnosis in a case of suspected stone, even if operation is not required. Furthermore, non-opaque stones are sometimes sufficiently large to demand operative removal. The presence of these stones can be inferred from descending pyelograms, and the stones themselves can be displayed by means of the opaque material they pick up in the course of a descending pyelography.

RÉSUMÉ.—Dans l'étude de cas suspects de calcul il s'agit (1) de ceux chez lesquels la radiographie donne une ombre visible, et (2) ceux où les rayons X ne donnent pas d'ombre.

Dans le premier groupe il faut déterminer la nature de l'ombre. Si elle représente un calcul il faut qu'elle soit exactement localisée dans des voies urinaires, et l'anatomie et la fonction des parties affectées et non affectées de l'appareil urinaire doivent être déterminées.

[1] *Postscript.*—Through the courtesy of Mr. Gordon-Taylor we have since learned that this patient is still alive and well—thirteen years after the operation.

On peut reconnaître les calculs par la forme typique qu'ils revêtent en grandissant dans le bassinet, dans un calyce ou dans l'uretère. Au commencement avant qu'ils aient pris leur forme caractéristique, on peut faire des radiographies pendant l'inspiration et pendant l'expiration. Des calculs intéressants peuvent se former dans les cas orthopédiques, ou dans d'autres cas immobilisés pour longtemps, et peuvent se désintegrer et passer par les voies naturelles, ou bien peuvent nécessiter une intervention chirurgicale.

Pour le diagnostic des calculs du rein et de la partie supérieure de l'uretère la pyélographie par la voie descendante est idéale. Pour le diagnostic des calculs infectés la voie rétrograde est préférable. Pour les petits calculs de l'uretère l'emploi du catheter opaque est la meilleure méthode.

Les calculs transparents aux rayons X ont une importance chirurgicale réelle. Il est absolument nécessaire de poser un diagnostic positif en cas de calcul suspect, même si une intervention n'est pas nécessaire. De plus, les calculs non opaques sont quelquefois assez grands pour nécessiter un traitement opératoire. L'existence de ces calculs peut être déduite au moyen de la pyélographie d'élimination, et les calculs mêmes peuvent être rendus visibles par la substance opaque qu'ils ramassent au cours d'une pyélographie d'élimination.

ZUSAMMENFASSUNG.—Die Untersuchung von Fällen von Verdacht auf Steine betrifft (1) solche, deren Röntgenbild einen Schatten aufweist, und (2) solche, bei denen die Röntgenuntersuchung keinen Schatten ergibt.

Bei der ersten Gruppe muss die Art des Schattens festgestellt werden. Wenn er einen Stein darstellt, so muss er genau in den Harnwegen lokalisiert, und Anatomie und Funktionszustand der beteiligten und unbeteiligten Abschnitte des Harntraktus müssen untersucht werden.

Steine können durch die eigentümliche Form, die sie bei ihrem Wachstum im Nierenbecken, in einem Kelch oder im Harnleiter annehmen, erkannt werden. In den früheren Stadien oder wenn die Form des Schattens nicht charakteristisch ist, können Röntgenbilder in Inspirations- und Exspirationsstellung angefertigt werden. Interessante Steine können sich bei orthopädischen und anderen Fällen, die durch lange Zeit hindurch immobilisiert waren, bilden; solche Steine können in der Folgezeit zerfallen und dann abgehen oder können eine chirurgische Behandlung notwendig machen.

Bei Steinen in der Niere oder im oberen Teil des Harnleiters ist die Ausscheidungspyelographie die ideale Untersuchungsmethode; bei infizierten Steinen ist die retrograde Methode besser; bei kleinen Uretersteinen ist die Verwendung eines Kontrastgebenden Katheters das beste Vorgehen.

Röntgendurchlässige Steine sind von einer erheblichen chirurgischen Bedeutung. Eine positive Diagnose muss bei Verdacht auf Stein gestellt werden, selbst wenn eine chirurgische Behandlung nicht erforderlich ist. Ueberdies macht bisweilen die Grösse solcher röntgendurchlässiger Steine ihre operative Entfernung notwendig.

Auf das Vorhandensein solcher Steine kann aus dem Ausscheidungspyelogramm geschlossen werden, und die Steine selbst können durch das Kontrastmittel, welches sie während der Ausscheidungspyelographie aufnehmen, sichtbar gemacht werden.

THE consideration of the X-ray pictures in cases of supposed urinary lithiasis may be discussed under two broad headings—(1) those pictures in which a shadow which may be a stone is present, and (2) those in which at first no such shadow is to be seen. It has been stated over and over again that only in the former of these two groups is the case of any surgical significance. This view, however, is open to two grave objections. Firstly, urology has reached a point of such accuracy in diagnosis that a positive answer is demanded to the question, "Is there any stone present?" Secondly, as will be shown, non-opaque stones may quite well be of such size as to demand operative removal.

The group in which the stone is opaque to X-rays comprises the great majority of cases. In these the duty of the surgeon is (1) to identify the shadow as being due to a stone, (2) to place the stone or stones accurately, and (3) to disclose the anatomical and physiological state of affairs in the part affected and in the urinary tract as a whole.

Diagnosis from " straight-through" X-rays.—Many shadows in appropriate areas may be recognized by their outline. For the most part, stones tend to grow to the shape of the cavities in which they lie. Thus a stone in the pelvis of the ureter becomes characteristically triangular. At a later stage it develops processes which grow out into the calyces, and a branched calculus results. Finally, such a stone may grow to fill the pelvis and calyces so completely as to resemble a perfect pyelogram. A solitary stone in a calyx tends to grow to the shape of a clove or dumb-bell, but this form is not often seen (fig. 1). A neglected stone in the ureter gradually becomes elongated and assumes the classical form so commonly illustrated.

This tendency for the stone to grow to the shape of the pelvis, for example, is very clearly shown in certain instances of the soft calculi which form during the prolonged immobilization of surgical tuberculosis and orthopædic patients. Of these stones some have later been observed to disappear when the patients are again up

FIG. 1.—A club-shaped stone growing in the lower calyx. This is a very characteristic and unmistakable shadow. This form is, however, not often seen in actual practice.

and about and X-ray records are available, demonstrating their gradual disintegration (figs. 2a and 2b). Others call for surgical interference and frequently present complex—and even desperate—problems. These calculi often appear to grow with astonishing rapidity, and although a lengthy period of recumbency is usual, quite a short illness is occasionally associated with the formation of stones (fig. 3).

Whilst in general, many stones throw characteristic shadows, a greater number are indefinite in outline, and various devices are employed to confirm their true nature. Of these one of the simplest and most reliable is to take photographs on deep inspiration and expiration. If at the limits of the excursion of the kidney the shadow retains its relationship to the kidney outline (usually this is best judged by measurement from the lower pole) it may fairly be assumed to be due to a renal stone. Similarly, if multiple shadows retain their relationship to one another it may be assumed that all are of the same nature. By this method reliable information may be obtained with a minimum of inconvenience to the patient.

Some confusion occurs in the case of ureteric stones in the upper fourth. Normally, no doubt, the ureter remains relatively fixed when the kidney moves, but when a stone is arrested in the upper fourth it will be found to move with the kidney. This is no doubt due to the œdematous infiltration of the wall of the

FIG. 2a.—A stone mass growing in the upper calyces of a patient immobilized on a frame for many months. Note particularly how the shadows outline the form of the calyces.

FIG. 2b.—The same case twelve months later. The patient had been up and about in the meantime and practically the whole of the shadow had disappeared.

Fig. 3.—A group of stones practically filling the pelvis and calyces of the right kidney in a patient who six months earlier had no stone shadows to be seen. At this time he had a partial gastrectomy and was in bed for just over two weeks. No other ætiological factor was discovered in this case. The urine was sterile and the stones were composed of earthy phosphates. The patient was admitted with severe colic and the diffuse nature of the calculi necessitated nephrectomy.

ureter and the tension of the urine within, which give it the rigidity of a distended hose-pipe (fig. 4).

Fig. 4.—Stone impacted in the upper 4th of the ureter with uroselectan dammed back causing rigid distension of the pelvis and ureter down to the level of the stone. Distension such as this with associated œdema is responsible for the movement, demonstrable on respiration, of calculi impacted in the upper part of the ureter.

The ordinary chronic calculous pyonephrosis is no exception to the general rule of movement on respiration, but in an acutely infected kidney, especially if associated with a perinephric abscess, all movement may be lost. In such cases the patient is confined to bed, the colon contains gas, and the kidney outline is invisible. The absence of movement in the stone shadows, which alone are visible, may, therefore, be misleading unless the observer is prepared for it.

Pyelography.—Pyelography by one or other route must be regarded as an essential in the investigation of every case of renal stone except : (1) in an emergency

FIG. 5.—A ureteric calculus in the upper part of the ureter demonstrated by means of an opaque catheter and injection of sodium bromide. Although the kidney was not infected uroselectan failed to show any shadow at all on this side owing to the complete degree of obstruction. Note that a more opaque pyelographic medium would have been better for demonstrating the ureter alone.

or ; (2) in a case calling frankly for nephrectomy. Only after pyelography can the approach to the stone be properly considered, the value of the kidney be assessed, and the appropriate technique worked out.

The intravenous route is agreeable to the patient and shows the whole tract at one examination. Moreover, judged with proper knowledge and circumspection, it is a valuable index of renal function. For non-infected stones in the " kidney " or upper ureter it is the method of choice. It has certain limitations and will fail to throw any shadow in : (1) a fairly complete ureteric obstruction (fig. 5); and (2) ureteric obstruction with infection (figs. 6a and 6b). Further, if accurate anatomical detail is required, a retrograde pyelogram will generally prove more satisfactory.

A curious phenomenon has been observed by Dr. J. H. Mather. In a proportion of cases examined by the intravenous route a dilatation of the ureter is observed below the level of the stone when the latter is at the uretero-pelvic junction or in
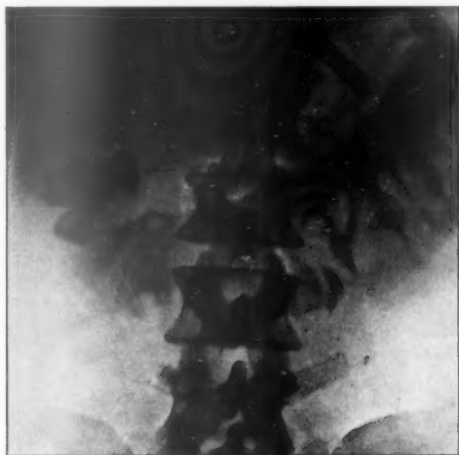
FIG. 6*a*.—Skiagram showing a stone in the pelvis of the right kidney, with diffuse hydronephrosis.

FIG. 6*b*.—The same case three years later: skiagram after injection of uroselectan, demonstrating (1) a remarkable recovery from a severe degree of hydronephrosis on the right and (2) failure to produce a shadow on the left side owing to infection despite the impaction of a calculus in the ureter.

the upper ureter. This occurs in the absence of any obstruction at a lower level, as though the ureter below the stone were in that state described by the physiologists as the " wave of relaxation which precedes the wave of contraction." The recognition

of this phenomenon is of some importance, since it may closely simulate organic obstruction at a lower level (fig. 7).

The retrograde route should be chosen in the presence of infection. Segregation is essential in such cases and pyelograms can conveniently be made at the same time.

Conflicting evidence may result in the same case from investigation by different methods. It is important to realize the possible differences between pyelograms obtained by different techniques. A retrograde pyelogram made with a highly concentrated and irritant solution causes spasm of the pelvis and results in a contracted shadow; a pyelogram obtained by the intravenous route will vary a little in size during the period of observation but will always be larger than that seen when the pelvis is in spasm; a retrograde pyelogram using a bland solution, such as 12½% sodium iodide, will commonly show a shadow much larger than either of the other two. Allowance should be made for these variations.

FIG. 7.—Stone at the uretero-pelvic junction showing a curious dilatation of the ureter below the level of impaction. There is no ureteric obstruction at a lower level.

Opaque ureteric catheterization.—For small shadows in the lower ureter the passage of an opaque catheter seems to be the method of choice. The bladder can be searched for other small stones and the ureteric orifice can be examined. The skiagrams should be stereoscopic if a positive diagnosis is to be made. Mistakes will certainly result from the assumption that superimposed shadows in a single film are thrown by bodies in contact with one another. This method of confirming the diagnosis has the additional advantage that catheterization often leads to the passage of the stone.

An exception may be made to this general rule in the case of ureteric stones which have lain in the lower end for a long time. Here, importance attaches to the assessment of damage done to the ureter and kidney, and back-pressure changes can certainly be very well judged by means of pyelography by the intravenous route.

Anatomical variations.—Double ureters and bifurcating ureters call for especial care in diagnosis. Pyelography by whichever route may lead to the filling of a half only of a " double " kidney. The half containing the stone may be missed.

But the appearances of such a pyelogram (fig. 8, ii) are so characteristic that there should be no difficulty in recognizing the anatomical condition. In a bifurcating ureter a uretero-pyelogram is all that is required to clarify the situation
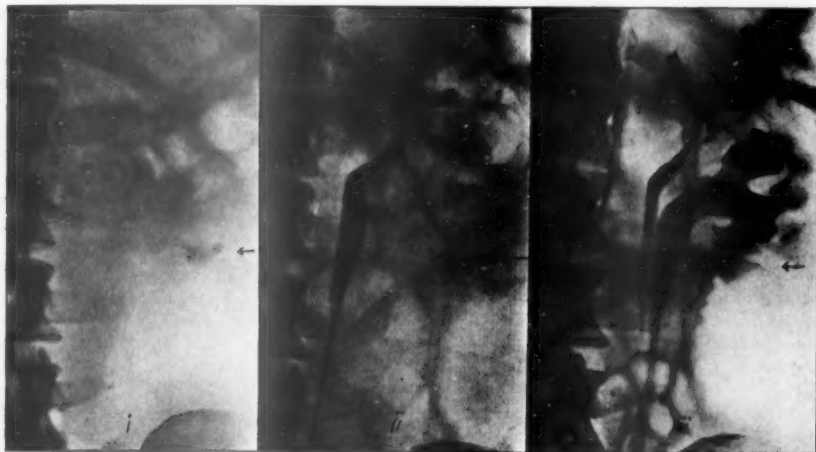
FIG. 8.—(i) Shadow in the region of the lower calyx of the left kidney.
(ii) Attempted pyelogram shows outline characteristic of part of a "double" kidney
(iii) Withdrawal of the catheter followed by a further injection demonstrates complete anatomical arrangement which results from a bifurcating ureter.

FIG. 9.—A typical ureteric stone with the catheter lying some distance from it. This proved to be a case of double ureter. The lower orifice was obscured by injection and œdema, but was revealed at a later date and the true diagnosis made.

(fig. 8, i, ii, and iii). In the case of a double ureter one orifice may easily be over-looked if the bladder base is injected, but a further search should disclose the true state of affairs (fig. 9).

MAY—UROL. 2 ✻

Diverticula of the ureter and pelvis are exceedingly rare and call for great tenacity of purpose in the resolving of conflicting items of evidence. Retrograde pyelography will usually be necessary (fig. 10).

Similarly, stones in ectopic and horse-shoe kidneys are responsible for shadows in unusual positions and call for persistence in investigation. The absence of a normal kidney outline should arouse suspicion.

Other atypical cases.—Stones may vary from type in special circumstances. Thus, in a hydronephrotic kidney a single stone may become large and rounded like a bladder stone and "jack-stones" may develop in the kidney pelvis under similar conditions. An alternative under the same conditions is for multiple calculi to form and grow to resemble a pocket of small round shot. These tiny stones, instead of becoming faceted, seem to rub against each other and to round off their corners like pebbles on the shore. Such a collection of small round stones throws a shadow which very closely resembles the mottling of a calcified lymphatic gland, from which it must be distinguished.

Difficulties in diagnosis.—It is sometimes necessary to employ every artifice and device before one can be quite certain of the nature of a shadow. Calcified glands in the line of the ureter constitute one of the principal difficulties, and the final diagnosis may be particularly hard to arrive at if the gland is adherent to the posterior parietal peritoneum in close contact with the ureter. If the opaque catheter can be passed beyond the level of the shadow a stereoscopic skiagram may be taken. If this is inconclusive some opaque material should be injected through the catheter, when it will be found that there is a partial hold-up with more or less dilatation above the level of the shadow, if it is a stone. If the fluid passes readily up to the kidney and records a normal pyelogram, without some dilatation or hold-up above the level of the shadow, it may be taken that the opaque object is a gland. Similarly, if the catheter will not reach the level of the shadow, an opaque fluid may be injected with caution. In the case of a normal ureter it is probable that the pelvis will be shown filled and that the ureter will throw no shadow. In the case of a ureteric stone the dye will either be arrested at the stone (fig. 5), or will pass beyond it and be shown as a collection in a more or less dilated ureter.

A final method of appeal in cases of this type is to take a lateral skiagram, when it will be seen that gland shadows lie well in front of the vertebral bodies. It is sometimes a help in cases which are still in doubt to make a lateral skiagram with an opaque ureteric catheter in position.

Great care needs to be exercised in the case of a ureter containing two or more stones. It is the rule that the lower of these stones is impacted, and that above it there is dilatation. Consequently the second stone is free to move and may be found in the ureter on one day and in the kidney on the next. A radiogram should invariably be made immediately before operation in cases of this type.

The problem of secondary hydronephrosis.—A stone impacted in the ureter leads to more or less hydronephrotic distension of the kidney. In going through the cases on which this paper is based, two facts have become evident in this connexion. Firstly, the kidney is capable of returning to a normal anatomical appearance after having been distended to a considerable degree (figs. 6a and 6b). Secondly, an enormous degree of hydronephrosis in a solitary remaining kidney is compatible with life and normal useful activity.

Non-opaque stones.—As has been argued at the beginning of this paper, non-opaque stones are of real surgical significance. In a case of suspected renal colic it is at the present time unsatisfactory to leave undecided the question of whether or not there is a stone present. Furthermore, non-opaque stones may on occasion be of considerable size and call for surgical removal.

These stones may be displayed in one of three ways. If a pyelographic medium is injected into the ureter or kidney, the stone may be displayed as a filling defect.
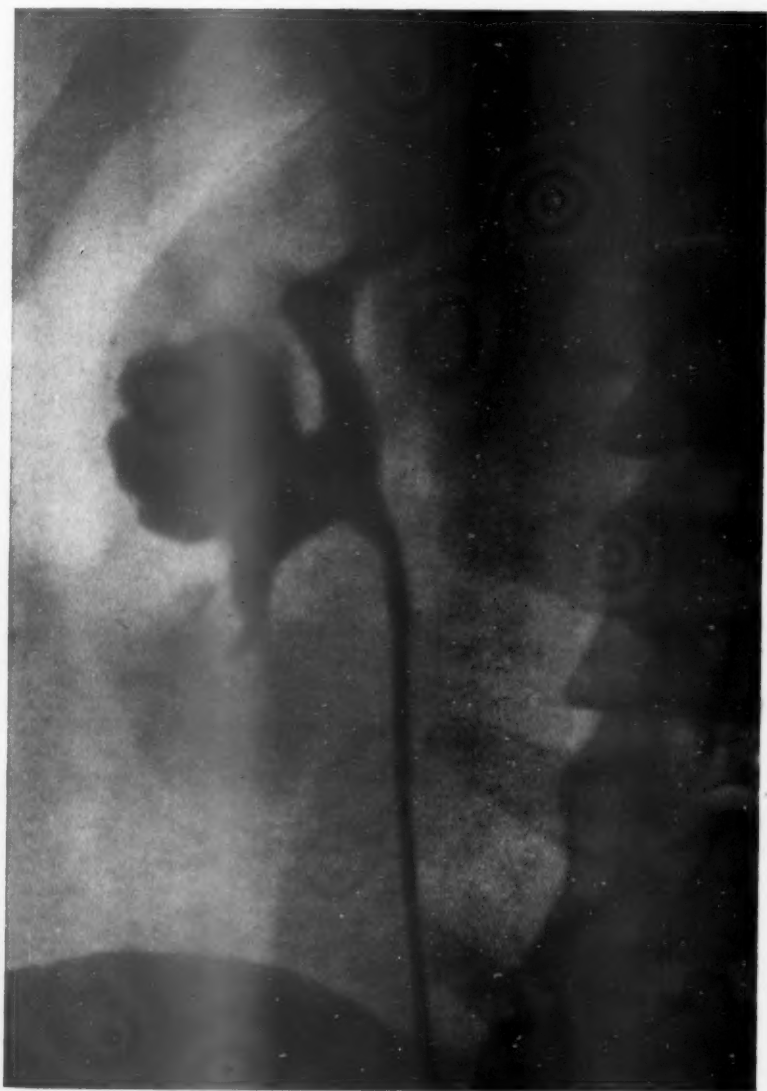
FIG. 10.—Retrograde pyelogram of a rare case of diverticulum opening from the middle calyx. This diverticulum contained many small rounded stones, of which the shadow closely resembled a calcified gland. With uroselectan a normal kidney had been demonstrated with very little opaque substance reaching the diverticulum.

This calls for very careful scrutiny of the films and, whilst a small stone may in this way be made visible in the ureter, only a stone of considerable size will be disclosed in the kidney (figs. 11*a* and 11*b*). It is said that, following the removal of the pyelographic medium, some may remain adherent to the stone and cause it to become visible. This is probably less likely to occur since the silver preparations have given way to sodium iodide.

Since the advent of intravenous pyelography new light has been thrown upon this subject. Firstly, it may be seen from a series of examinations spread over a period of time that the function of a suspected kidney is becoming progressively poorer. This should lead the observer to renewed efforts to discover some satisfactory explanation for the colic complained of and the lessening function. Secondly,

FIG. 11*a*.—Skiagram of pelvis (in which no stone shadow was to be seen) following injection of uroselectan. No stone shadow has been revealed. The degree of "hold-up" in the ureter is not abnormal. Evacuation of the bladder did not bring to light any fresh facts.

FIG. 11*b*.—Ureterogram in the same case showing filling defect due to non-opaque stone. This examination was made because repeated examinations with uroselectan showed rapidly diminishing renal function. They did not, however, demonstrate the presence of a stone.

where a non-opaque stone is impacted in the ureter the descending pyelographic medium may be seen to be arrested in all films at a certain point. If the picture is always the same it may be assumed that the arrest is not due to a normal wave of contraction and an organic cause for obstruction may be postulated.

Further careful scrutiny of the films will probably lead to the discovery of the third phenomenon. This is the staining of the stone by means of the intravenous pyelographic medium. Commonly, stone shadows are seen to be denser following uroselectan, and in certain cases in which a calculus has not previously been visible it will be found that a few hours, or even a day or two, after the injection, at a

time when the rest of the tract is free from dye, a stone shadow is to be seen. In the series under discussion this phenomenon has been responsible for the disclosing of no less than five calculi. Of these, one was a small one in a horseshoe kidney, two were small stones in the lower end of the ureter (figs. 12a and 12b), which have since been passed, and two were stones at the lower end of the ureter requiring operative removal. Unfortunately none of the small stones were recovered, but it seems probable that they were composed of uric acid. Of the two stones removed by operation, one was an inch long and a third of an inch in diameter and the other, of very irregular shape, measured roughly a quarter of an inch in every direction.
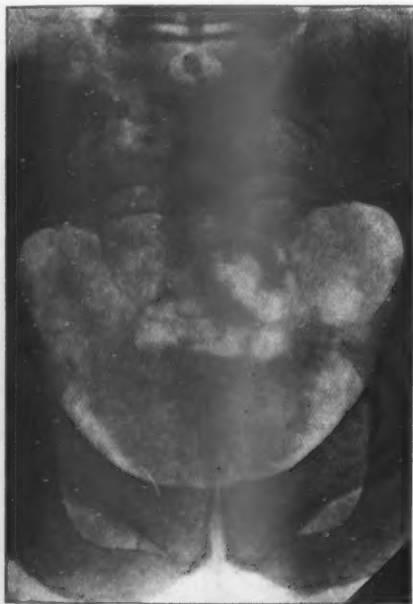
FIG. 12a.—Skiagram of pelvis, showing no stone shadow.

FIG. 12b.—The same case some hours after a uroselectan examination. The shadow of a small stone at the lower end of the left ureter is now visible.

The three non-opaque stones recovered by operation (figs. 11, 13, and 14) were examined and their composition was reported as follows: The first, ammonium urates in the centre with some earthy phosphates; at the periphery earthy phosphates and some urates. The second, chiefly some organic substance which did not give the spectroscopic appearance of blood; with this, traces of calcium oxalate and magnesium phosphate; uric acid was not found. The third, earthy phosphate with some calcium oxalate in the extreme periphery.

Although indirect references have been made to the subject, it would appear that insufficient attention has been drawn to the importance of intravenous pyelography in the elucidation of the problems presented by non-opaque calculi. It would seem that their incidence represents something between 2% and 10% of all stones, as estimated by various writers in different parts of the world. In this series they

Fig. 13a.—Skiagram of pelvis, showing bladder outlined by calcification resulting from bilharzia many years before.   No stone shadow is visible.

Fig. 13b.—The same case four hours after an examination with uroselectan B.   A stone is now visible in the right ureter.   This was subsequently removed by open operation. (*See* text.)

Fig. 14*a*.—Skiagram of pelvis in another case presenting symptoms of ureteric stone. No stone shadow is visible.
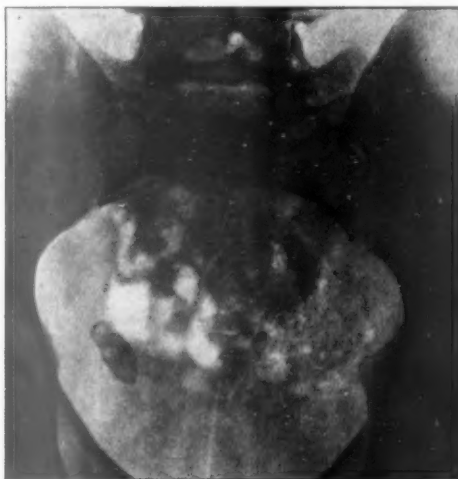
Fig. 14*b*.—The same case some hours after the injection of uroselectan B. A large stone is now visible in the lower end of the right ureter, where it is outlined by the opaque substance which adheres to its surface. This stone was subsequently removed by open operation. (*See* text.)

represent roughly 5% of the cases and it is clear that they can no longer be disregarded with equanimity.

[Thanks are due to Dr. J. H. Mather, Dr. R. E. Roberts, Dr. Norah Walker, Dr. Fox and other members of Radiological Departments, without whose assistance this paper could not have been compiled.]

**Radiographic Diagnosis of Renal Growth and Renal Calculus :
Demonstration of Lantern-slides.**—H. P. WINSBURY-WHITE, F.R.C.S.

(1) *Renal growths.*—A kidney showing hypernephroma with a diameter of about an
inch.   It was only owing to the presence of a stone in the pelvis that the growth was
discovered at operation.   In spite of the small dimensions of the tumour, microscopy
showed that malignant cells had already extended through the capsule which com-
pletely surrounded the neoplasm.   It was twelve years ago since this kidney was
removed, and the patient was at present alive and well.

(2) *A series illustrating the uncertainty which may arise in interpreting lateral
radiograms.*—One skiagram taken in the lateral position showed a series of opacities
lying one above the other in front of the bodies of the vertebræ.   The uppermost of
these shadows in the antero-posterior skiagrams suggested the possibility of a renal
calculus.   In the lateral skiagram, however, the presence of other shadows lying
below the first and well in front of the bodies of the vertebræ strongly suggested that
the uppermost shadow was due to a calcified gland.

A subsequent slide showed a ureteric catheter passing up to the kidney on the
side in question, and demonstrated that the catheter and the uppermost shadow
came into intimate contact, thus proving that the latter was a renal calculus.

A slide of a drawing of the kidney which had been hardened after removal,
illustrated the reason why the shadow of the renal calculus lay so far in front of the
bodies of the vertebræ in the lateral picture.   The stone was seen to be in the pelvis
of the kidney, which was in a state of very considerable distension, thus causing the
calculus to be moved well forward.

Section of Therapeutics and Pharmacology

President—J. H. BURN, M.D.

[*February 12, 1935*]

Pituitary Cachexia with Disturbance of Circulatory Regulation. Result of Treatment with Prolan.

By Professor C. STANTON HICKS, M.B., and F. SANDILAND HONE, M.B.

(From the Department of Human Physiology and Pharmacology, University of Adelaide).

ABSTRACT.—A case of extreme wasting associated with amenorrhœa for eighteen months. On finding that the subject showed a fall of blood-pressure with unaltered pulse-rate on sitting up, anterior pituitary dysfunction (Simmonds' syndrome (?)) was diagnosed and prolan (Bayer) was administered. Following 100 units intramuscularly administered, the circulatory response became normal in twenty-four hours. The pulse rapidly improved in strength and all circulatory symptoms disappeared within a week. Weight increased at first rapidly, and the nutrition, skin and hair improved remarkably. Metabolism of sugar, as shown by glucose tolerance tests, became normal, and evidence for improvement in fat metabolism is brought forward.

The study of the case goes to support the conclusion of Schellong that a function of the anterior pituitary is to influence the circulatory response to muscular effort. That hypotonia of itself is not responsible for the circulatory symptoms is shown by the failure of ephedrine (which raised the blood-pressure) to remove the circulatory symptoms.

Contrary to some accepted beliefs, prolan, which is prepared from urine of pregnant mares, has a profound metabolic effect, as well as an effect on the ovary. The diagnostic value of the circulatory response in doubtful cases is discussed.

RÉSUMÉ.—Cas de cachexie extrême avec aménorrhée persistant depuis 18 mois. Suivant l'observation que la pression sanguine de la malade tombait quand elle se soulevait, sans changement de la vitesse du pouls, on fit le diagnostic de dysfonction du lobe antérieur de l'hypophyse (syndrome de Simmonds ?), et un traitement par le prolan (Bayer) fut institué. Suivant l'administration de 100 unités par la voie intramusculaire, la réponse circulatoire devint normale en 24 heures. Le pouls devint rapidement plus vigoureux, et tous les symptomes circulatoires disparurent en moins de huit jours. Augmentation du poids, rapide au commencement, et grande amélioration de la nutrition, et de l'état de la peau et de la chevelure. Le métabolisme du sucre, mesuré par la tolérance du glucose, devint normal, et il y a de l'évidence que le métabolisme de la graisse s'est amélioré.

L'étude de ce cas supporte la conclusion de Schellong qu'une des fonctions du lobe antérieur de l'hypophyse est la régularisation de la réaction circulatoire à l'effort musculaire Le fait que l'éphedrine (qui produit une hausse de la pression sanguine) n'a pas produit d'effet sur les symptomes circulatoires montre que l'hypotonie seule n'est pas la cause de ces symptomes.

Contrairement à certaines opinions acceptées, le prolan, une préparation obtenue de l'urine de juments gravides, possède un grand effet sur le métabolisme aussi bien que sur l'ovaire. Les auteurs discutent la valeur de la réponse circulatoire dans le diagnostic des cas douteux.

ZUSAMMENFASSUNG.—Fall von hochgradiger Kachexie mit Amenorrhöe seit 18 Monaten. Nach der Beobachtung dass beim Aufsitzen der Kranken der Blutdruck sank, während die Pulsgeschwindigkeit unverändert blieb, wurde Dysfunktion des Hypophysenvorderlappens diagnostiziert (Simmonds'sche Krankheit ?), und prolan (Bayer) gegeben. Nach Zufuhr von 100 Einheiten intramuskulär wurde die Kreislaufreaktion in 24 Stunden wieder normal. Der Puls wurde rasch stärker, und alle Zirkulationsstörungen sind binnen 8 Tagen verschwunden. Anfangs rasche Gewichtszunahme, und merkwürdige Besserung der Ernährung, der Haut und der Haare. Der Zuckerstoffwechsel, durch Glukosetoleranzversuche bestimmt, wurde normal, und Beweis für die Besserung des Fettstoffwechsels wird gebracht.

Die Befunde in diesem Fall sprechen für die Annahme Schellongs dass eine der Funktionen des Hypophysenvorderlappens die Beeinflussung der Reaktion des Kreislaufs auf Muskelarbeit ist. Dass die Kreislaufsstörungen nicht nur auf Hypotonie zurückzuführen sind, geht aus der Tatsache hervor, dass sie durch Ephedrin (die der Blutdruck erhöhte) nicht beseitigt wurden.

Im Gegensatz zu anerkannten Meinungen besitzt das Prolan einen starken Einfluss nicht nur über die Ovarien sondern auch über den Stoffwechsel. Die diagnostische Bedeutung der Kreislauf-Reaktion in zweifelhaften Fällen wird besprochen.

IN many diseases known to be associated with pituitary dysfunction, such as dystrophia adiposa genitalis, hypopituitary infantilism, acromegaly, hypopituitary adiposity, etc., there is manifested some departure from the normal metabolism, at least as such is indicated by the basal metabolic rate, or specific dynamic response. Since the anterior lobe of the pituitary body is involved in some degree in these conditions, we might expect to find that modern therapeutic use of the anterior pituitary hormone would confirm the expectation of some metabolic effect.

Some evidence favouring this view was brought by Kohler [14] but the considered opinion of the Bayer scientific staff, as expressed in their summary (with literature) supporting the therapeutic indications for prolan, is contrary to this view.

Animal experiments to prove the influence of anterior pituitary hormone upon specific dynamic response have given equivocal results (Kestner [11] Reiss and Winter [19]) whilst Bernstein and Falta [1] reported a lowering of the basal metabolic rate following clinical administration of an anterior pituitary preparation. This effect of lowering the basal metabolism was shown by Hertzfeld and Frieder [6] to be associated with increased specific dynamic response, in cases where the same was lowered or absent. In normal cases or cases of pathological obesity, Knipping [13], Kestner, Liebeschütz-Plaut, and Schadow [11] obtained a lowered specific dynamic response but confirmed the previous workers' results, which were again substantiated by Liebesny [16]. These latter workers also used a true anterior pituitary extract. The question which affects us in the present instance, is whether prolan, which is obtained from mares' urine, and contains, according to Zondek [23] the sex hormone (as distinct from other hormones present in the anterior pituitary) contains also one which influences the specific dynamic reaction to assimilated foodstuffs. Both Aschheim and Zondek [22] believe in the separation of these two effects, if not actually in the existence of two hormones.

The preparation used for therapeutic purposes in the present instance was prolan (Bayer), which is prepared by the method of Zondek [23] by precipitation from the urine of pregnant mares on addition of ether, or other lipoid solvents. By means of alcohol the "anterior pituitary" hormone is again precipitated from aqueous solution, in which it has been taken up after the first stage. After further purification, only the water-soluble portion is used. In our experience we find no

difference in action between that of our own preparation from human pregnancy urine, and that of prolan. One of us (C. S. H.) was present at the Weisbaden Congress 1930 when Schellong [20] reported a case with a peculiar condition of the circulatory system, which did not respond normally to increased circulatory demands due to muscular effort. He later [21] reported at length on a series of such cases, including the first-mentioned, and from a study of these cases it appears that whatever other symptoms and signs of "pituitary" disturbance may be present, if the normal circulatory response to muscular effort is weakened or absent, there is an involvement of a specific function of the anterior lobe of the gland.

The case which is the main subject of this report was under observation by F.S.H. for some years, and a clinical summary is given below.

Miss A. J. Born 1910. Childhood healthy. Asthma when 10 months old.

1916.—Whooping-cough, no more asthma, but had attacks of sneezing at age of 9; nose cauterized.

1928.—Entered bank in September as typist.

1929.—Nasal catarrh in April.

1930.—February, nose cauterized; April, asthma; July, operation on nose; bone removed. Asthma worse, every night and in the day.

1931.—Mumps in December. Ill two weeks.

1932.—April to July. Attacks of asthma frequent and severe. Losing weight. Tired and knocked-up. Weight 8 st. 2 lb.
     August. Sudden amenorrhœa; monthly periods previously regular and normal. *Asthma ceased.*
     September. Given iron; indigestion resulted.
     November. One month's leave. Thyroid 1 gr. a day. Lost 1 lb. in a week. Cod-liver oil, malt extract, ovaltine. Went on losing weight till January 1933.

1933.—Gained 5 lb. from January to June. Had influenza at end of August. Lost 5 lb. in week.
     December. Weight down to 7 st. 10 lb.

1934.—March 15. On examination: Thin, bright and active. Weight 6 st. 10 lb. Pulse 42 (regular). Heart sounds pure. B.P. 100/60. Heart, lungs and abdomen normal. Axillary hair scanty. Skin dry. Reflexes sluggish. Rectal examination showed uterus in normal position. Nothing abnormal in fornices.
     March 22. Weight 92 lb. Urine: no sugar. Pulse 51 sitting. B.P. 100/60 sitting.
     April 4. Pulse 60 sitting. B.P. 105/70 sitting.
     April 7. Weight 92 lb. Pulse 51 sitting. B.P. 100/60 sitting. Tab. ephedrin 0·03 grm. t.d.s.
     April 9. Pulse 96 sitting. B.P. 130/80. Ephedrin reduced to 1 tab. daily. Ac. hyd. dil. fer. et. am. cit. mixture given.
     April 11. Pulse 66 sitting. B.P. 108/80.
     April 19. Pulse 72 sitting. B.P. 110/80. Ephedrin 2 tabs. daily.
     May 16. Weight 84 lb. Pulse 72 sitting. B.P. 110/90. Given three months' leave. May 26.
     June 14. Weight 84 lb. Pulse 72 sitting. B.P. 110/90.
     June 21. Urine: no sugar. Pulse 56 lying. B.P. 105/80 lying. Put to bed.
     June 30. Pulse 60 lying. B.P. 105/80 lying.
     July 7. Pulse 66 lying. B.P. 105/90 lying. Pressure difficult to determine.
     July 12. Pulse 72 lying. B.P. 108/90. Insulin and glucose once.
     July 16. Pulse 60 lying. B.P. 105/85 lying. Strychnine and belladonna.
     July 21. Pulse 56 lying. B.P. 105. Electrocardiogram. Blood-pressure difficult. Ephedrin discontinued.
     July 24. Weight 73½ lb. Pulse 56 lying, 60 sitting. B.P. 105 lying, 90 sitting. Professor Hicks consulted. B.P. doubtful.
     July 26. Pulse 56 lying, 66 sitting. B.P. 104 lying, 95 sitting. Hypo. prolan 100 units, 10 a.m.
     July 27. Pulse 76 lying, 92 sitting. B.P. 98 lying, 107 sitting. Pulse 66 lying, 90 sitting. B.P. 90 lying, 98 sitting one and half hours later.

1934.—July 28.   Pulse 64 lying, 67 sitting.   B.P. 95 lying, 100 sitting.   Hypo. prolan 100 units.
   July 29.   Pulse 60 lying, 80 sitting.   B.P. 105/80 lying, 112/85 sitting.
   July 30.   Sat up for two hours.   Given prolan at 9 p.m.
   July 31.   At 9.30 a.m. pulse 64 lying, 80 sitting.   B.P. 87 lying, 92 sitting.
      At 6.30 p.m. pulse 58 lying, 72 sitting.   B.P. 95 lying, 100 sitting.
      R.B.C. 5,025,000 slight variation.   W.B.C. 8,250.   No abnormal cells.   Relative number normal.   Hb. 85%.
   August 1.   Weight 73¾ lb.   Pulse 72 lying.   Urine, no sugar.   Daily injections 100 units prolan started.   Calories 973.
   August 2.   Pulse 82 lying.   Calories 1087 (intake).
   August 3.   Calories 1371 (intake).
   August 4.   Calories 1419.   Pulse 82 lying.
   August 5.   Calories 1432.   Pulse 80 lying.
   August 6.   Calories 1456.   Pulse 76 lying, 96 sitting.   B.P. 92 lying, 98 lying again.
   August 7.   Calories 1499.   Pulse 93 lying, 124 sitting, 81 lying again.   B.P. 98/68 lying, 99/80 sitting, 99/70 lying.
   August 8.   Calories 1520.   Weight 76½ lb.   Pulse 80 lying, 96 sitting, 80 lying.   B.P. 94/76 lying, 98/80 sitting, 94/76 lying.
   August 9.   Calories 1080.   Pulse 80 lying, 92 sitting.   B.P. 92/70 lying, 96/70 sitting.   Blood-sugar curve (*see* graph, p. 61).
   August 10.   Calories 1459.   Pulse 72 lying, 88 sitting, 74 lying.   B.P. 99/64 lying, 99/70 sitting, 91/62 lying.
   August 11.   Calories 1204.   Acid and strychnine mixture restarted.
   August 12.   Calories 1385.   Pulse 72 lying, 92 sitting, 70 lying.   B.P. 84/60 lying, 90/70 sitting, 84 lying.
   August 13.   Calories 1247.   Pulse 66 lying, 87 sitting.   B.P. 90/60 lying, 96/66 sitting.
   August 14.   Calories 1445.
   August 15.   Calories 1449.   Weight 78½ lb.   Pulse 72 lying, 108 sitting, 78 lying.   B.P. 99/64 lying, 84/70 sitting, 88/62 lying.
   August 16.   Calories 1369.   Pulse 72 lying, 84 sitting.   B.P. 92/60 lying, 100/80 sitting.   Tongue clean.
   August 17.   Calories 1324.
   August 18.   Calories 1279.
   August 19.   Calories 1404.   Pulse 60 lying, 78 sitting.   B.P. 90/70 lying, 90/74 sitting.
   August 20.   Calories 1461.
   August 21.   Calories 1323.
   August 22.   Calories 1269.   Weight 79¼ lb.   Pulse 60 lying, 84 sitting.   B.P. 90/60 lying, 85/60 sitting.
   August 23.   Calories 719.   Sugar in urine after 50 grm. glucose.
   August 24.   Calories 1283.   No sugar in urine.   Pulse 64 lying, 80 sitting, 64 lying.   B.P. 90/60 lying, 100/70 sitting, 94/70 lying.
   August 25.   Calories 1026.
   August 26.   Calories 1125.   Pulse 60 lying, 78 sitting, 60 lying.   B.P. 90/60 lying, 94/70 sitting, 90/60 lying.
   August 27.   Calories 1178.   Pulse 66 lying, 96 sitting, 75 lying.   B.P. 84/44 lying, 84/60 sitting, 92/58 lying.
   August 28.   Calories 990.   Pulse 58 lying, 76 sitting, 60 lying.   B.P. 90/60 lying, 96/70 sitting, 90/60 lying.
   August 29.   Calories 1178.   Weight 79 lb.
   August 30.   Calories 1123.   Pulse 56 lying, 76 sitting, 56 lying.   B.P. 90/60 lying, 96/70 sitting, 90/70 lying.
   August 31.   Calories 1227.
   September 1.   Calories 1200.   Prolan injections daily.   Prolan by mouth started daily in addition.
   September 2.   Calories 1119.
   September 3.   Calories 1165.
   September 4.   Calories 1165.   Pulse 59 lying, 90 sitting, 54 lying.   B.P. 80/35 lying, 85/60 sitting, 75/50 lying.

1934.—September 5.   Calories 1142.   Weight 80 lb.
    September 6.   Calories 1257.
    September 7.   Calories 1355.   Pulse 56 lying, 72 sitting, 56 lying.   B.P. 90/60 lying, 96/70 sitting, 90/50 lying.
    September 8.   Calories 1257.
    September 9.   Calories 986.   Pulse 60 lying, 84 sitting, 58 lying.   B.P. 90/60 lying, 96/70 sitting, 90/70 lying.
    September 10.   Calories 960.
    September 11.   Calories 981.   Allowed up.
    September 12.   Calories 1228.   Weight 80½ lb.   Pulse 50 lying, 75 sitting, 54 lying.   B.P. 88/30 lying, 96/70 sitting, 88/60 lying.   Prolan dragees left off.
    September 13.   Calories 1195.   Left hospital.   Exercise increased.
    September 15.   Acid mixture omitted.
    September 27.   Weight 81½ lb.   Pulse 46 lying, 60 sitting, 49 lying.   B.P. 103/70 lying, 106/80 sitting, 93/58 lying.   After journey from Glenelg.
    October 11.   Weight 81¾ lb.   Pulse 42 lying, 48 sitting, 48 lying.   B.P. 100/65 lying, 104/70 sitting, 96/70 lying.   Hair which started growing more in hospital is still growing.   States nails more brittle ; no ridging.   Tongue dirty again, acid mixture given.
    October 19.   Weight 81¾ lb.   Pulse 60 lying, 66 sitting.   B.P. 94/60 lying, 100/70 sitting.   Tongue cleaner.   Preloban by mouth substituted for injections of prolan (3 tabs. a day).
    October 25.   Weight 82 lb.   Pulse 48 lying, 52 sitting.   B.P. 86/50 lying, 92/60 sitting.
    November 2.   Weight 82 lb.   Pulse 54 lying, 72 sitting, 54 lying.   B.P. 100/65 lying, 102/65 sitting, 96 lying.   Feeling better ; more vitality, but amenorrhœa persists.

When the patient was first seen by C. S. H. the pulse was extremely weak, and it was very difficult to secure blood-pressure-readings even by palpation.   When the patient was assisted into a sitting-posture—exerting herself to her capacity—her blood-pressure fell, and she complained of giddiness and diplopia.   Neither symptom, it might be thought, would be unexpected in so emaciated a subject, but it will be noted that the pulse-rate has increased only some 18%.   The patient though in a warm bed, was heavily clad in three layers of garments, complained of the cold, and could sleep only fitfully at night.   From the general cachectic appearance, the "dead-goose skin"—as the patient herself described her inelastic cutaneous tissues— the brittle lifeless hair, low metabolism, amenorrhœa and severe constipation, together with the suggestive type of circulatory response, anterior pituitary dysfunction was diagnosed.   The patient was moved to hospital, and 100 units of prolan were administered intramuscularly.   The effect on the vascular response was noted twenty-two hours after administration.   The blood-pressure rose on the patient's sitting up—instead of falling ; she felt subjectively better, slept better, and did not complain of the cold.

During the first week the objective changes were perhaps most remarkable, as they were so rapid.   Food was eaten with greater relish, the dose of cathartic (senna) to which she had become addicted, was halved, and the pulse became daily more vigorous.   This latter was an outstanding feature.   When during the first week of treatment, the patient sat up in bed, the pulse though fuller, showed transient irregularities typical of ectopic beats ; giddiness and diplopia never recurred after the ingestion of the first 100 units of prolan, and though the patient, previous to entering hospital, could not stand unaided without giddiness and weakness, she could be assisted to the bathroom, and similarly return, after a hot bath, with no circulatory distress whatever, forty-eight hours after the first injection.   The tongue rapidly cleared, and after the second injection the skin had already become soft and elastic, and the mask-like aged appearance of the face had softened.

The circulatory response having once changed its sense, it retained its character. The subsequent circulatory changes were the progressive increase in pulse-volume and elasticity, and degree of acceleration on sitting-up. It was found too, that if the patient were examined immediately on resuming the recumbent posture, the blood-pressure often sank below the original lying value, and that the diastolic pressures were often widely varied. (*See* e.g. September 27 : " Lying 103/70 mm. Sitting 106/80.   Lying 93/58.")

It is clear that we are here dealing with a circulatory change which does not depend on a recovery of general bodily strength, and that the circulatory response to prolan administration, was evidence that the original " effort test " had diagnostic value in this instance.   This point is the more important as the range of defective response, and variety of associated signs and symptoms, c.f. Schellong [20], makes it impossible to give a descriptive name to anything other than the circulatory syndrome itself.

Schellong may here be quoted with some advantage.

" These extraordinary symptoms, i.e. circulatory collapse, are noted in several cases of the disease, but only as short and sudden loss of consciousness, or as a condition of weakness.   They have not been explained by Simmonds [21], Fahr [4], Lichtwitz [17], Jakob [10], Hoesslinger and Stricker [9] and other observers.   They depend on the circulation.   They are not to be ascribed simply to the low blood-pressure which is so often a symptom of Simmond's disease.   Even in the literature we find cases where the blood-pressure is normal, Fahr [4], or raised, Hirsch and Berberich [8], in which unusual attacks of vertigo are noted.   According to my observations there may be daily variations in blood-pressure.   The real cause of the collapse is much more a disturbance in circulatory regulation when extra calls are made upon the circulation."   Schellong was able to demonstrate that although adrenalin would raise the blood-pressure, the circulatory response to effort still resulted in a fall of blood-pressure.   In these disturbances we are dealing with something more than the hypotonia with fixed pulse-rate, seen in certain pituitary disorders.

Schellong also demonstrated that anterior pituitary extract could mitigate or entirely remove these circulatory disturbances.   Posterior pituitary extract is without effect.   In the case under review, the circulatory defect was successfully cured while there was still present a high degree of emaciation, cf. Schellong [20].

Metabolic effect of treatment.—The attempt to increase calorific intake disclosed a curious fact of importance in the understanding of the metabolism of fat.   Attempts to increase body-weight in the earlier stages of the disorder, were frustrated by the patient's absolute antipathy to fat in any form.   Potatoes too she could not eat, for not only did they taste " like sawdust " but they caused violent indigestion.   Fat had always been eaten sparingly, but with the onset of the disease it could not be taken at all.   The week following the administration of the first 100 units of prolan, the patient found her antipathy to fat definitely diminished, and it soon became apparent that our difficulty in increasing her weight was a matter of total intake and was not as before, aggravated largely on the absence of fat from her diet. Potatoes however were still rejected.   From the body-weights given, it will be seen that the gain under treatment was remarkable, and if as is likely, the alimentary organs are small and hypofunctional, the cause of the feeding difficulty is obvious. We are satisfied that we are dealing with an altered response to fat as a separate article of diet, and that prolan has influenced this.   The following tests were made to investigate the metabolism : (1) Glucose tolerance test prior to prolan therapy, 9.8.34 ; (2) glucose tolerance test after prolan, 23.8.34 ; (3) response to adrenalin after prolan, 13.9.34.   (In this the patient experienced absolutely no subjective

symptoms.)   The results show that the carbohydrate metabolism had been influenced by prolan, and that sugar mobilization due to adrenalin was normal.

Fat metabolism was studied, 6.9.34, by estimating the respiratory quotient.   In the post-absorptive state R Q = 0·58; after breakfast at 11 a.m., with patient sitting up in bed R Q = 0·68.   At 2.30 p.m., after lunch at 1.30 p.m., and after patient had walked upstairs to sun-balcony and was at rest in a comfortable chair, pulse and respiratory rates being constant over a period of five minutes, R Q = 0·94.

The basal metabolic rate calculated on a fat-R Q basis was − 20%.

The low morning respiratory quotient can be compatible only with conversion of carbohydrate into fat.   Further investigation on these lines is in progress, but enough has been done to show that the metabolism of fat is involved as well as that of carbohydrate, and that prolan influences both.   It may be significant that from childhood the patient did not readily eat much fat, and that with the onset of the wasting and amenorrhœa, an aversion to fat became manifest.   Was there, in
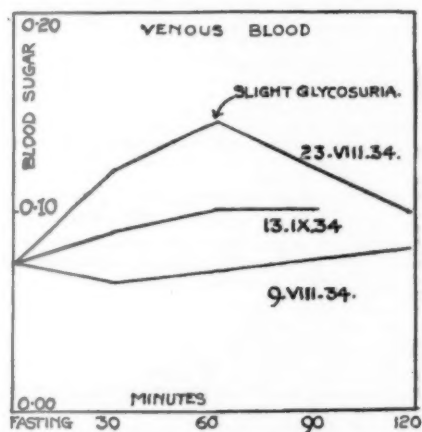
9.8.34 and 23.8.34.   Glucose tolerance tests using 50 grams glucose.
13.9.34.   0·5 c.c. 1/1000 adrenalin injected subcutaneously.

fact, some low order of anterior pituitary function, which became gradually pathological when the sex-cycle was fully established, or was the attack of mumps the cause of a loss of pituitary function in an already hypofunctioning gland, directly or indirectly ?

Summary.—The present case gives support to the conclusion of Schellong that the anterior pituitary lobe influences in some potent manner the response of the vascular system to increased circulatory demand as made by muscular effort.   The experimental pituitary extirpation work of Cushing [3] and the capillary observations of Bock [2] in relation to the action anterior pituitary hormone, are supported by the work of Schellong, and point to some peripheral effect of an anterior pituitary hormone on the circulation.   Peripheral dilatation of the vessels would explain the fall of blood-pressure on exertion, and Schellong has proved the co-existence of abnormal capillary calibre in 60% of cases of hypertonic vasoneurosis of the young, in which exertion causes a fall in diastolic pressure.   In what manner the heart-beat is influenced is at yet difficult to see, but it may be that the hormone influences the

dynamic response of cardiac muscle. The early symptoms of circulatory insufficiency in Addison's disease are related more to lack of circulatory response, than to the absolute height of the systolic pressure, and a study of two cases by Hicks and Mitchell in which a modification of therapeutic methods is described, points in this direction. Kraus has in fact demonstrated profound changes in the pituitary gland in Addison's disease, and the experimental work of Müller and Bock [18], and of Heller [5], as well as that of recent investigations upon the thalamus, e.g. Le Gros Clark, suggests a functional relation between the pituitary and the vasomotor system.[1]

There is strong evidence in favour of an influence of prolan (pituitary sex hormone of Zondek) on the metabolism of both carbohydrate and fat, and of the curative value of prolan therapy in certain cases of pituitary cachexia, at all events, when associated with altered circulatory response to effort. The therapeutic results of the change from prolan to preloban, though favourable, are to date insufficient to form a basis for conclusion.

Our thanks are due to Dr. F. Ray Hone for assistance with the blood-sugar examination.

REFERENCES

1 BERNSTEIN u. FALTA, *Kongr. f. inn. Med.*, 1912, xxix, 536.
2 BOCK, *Zeit. exper. Med.*, 1930, lxxii, 561.
3 CROW, CUSHING, and HOMANS, *Quart. Journ. Exper. Physiol.*, 1909, ii, 389; *Lancet*, 1910, clxxviii, 1707.
4 FAHR, *Deutsche med. Wchnschr.*, 1918, xliv, 206.
5 HELLER, *Arch. f. Exper. Path. u. Pharmakol.*, 1933, clxxiii, 1291.
6 HERTZFELD and FRIEDER, *Z. physik. Therap.*, 1928, xxxv, 149.
7 HERMANN, *Klin. Wchnschr.*, 1928, vii, 944.
8 HIRSCH and BERBERICH, *Klin. Wchnschr.*, 1924, iii, 483.
9 HOESSLINGER and STRICKER, *Frankf. z. Path.*, 1932, xxix, 492.
10 JAKOB, *Virchow's Arch.*, 1923, ccxlvi, 151.
11 KESTNER, *Verh. dtsch. Ges. f. inn. Med.*, 1922, xxxiv, 339.
12 KESTNER, LIEBESCHÜTZ-PLAUT, and SCHADOW, *Klin. Wchnschr.*, 1926, v, 1646.
13 KNIPPING, *Deutsche med. Wchnschr.*, 1923, xlix, 12.
14 KOHLER, *Klin. Wchnschr.*, 1930, iii, 110.
15 KRAUS, *Virchow's Arch.*, 1923, ccxlvii, 421.
16 LIEBESNY, *Biochem. Zeit.*, 1924, cxliv, 308.
17 LICHTWITZ, *Klin. Wchnschr.*, 1922, ii, 1877.
18 MÜLLER and BOCK, *Deutsche med. Wchnschr.*, 1929, lv, 1291.
19 REISS and WINTER, *Endokrinologie*, 1929, iii, 3.
20 SCHELLONG, *Verh. dtsch. Ges. inn. Med.*, 1930, xlii, 62; *Klin. Wchnschr.*, 1931, iii, 100.
21 SIMMONDS, *Deutsche med. Wchnschr.*, 1914, xl, 322.
22 ZONDEK and ASCHHEIM, *Arch. Gynäk.*, 1927, cxxx, 1.
23 Id., *Klin. Wchnschr.*, 1928, vii, 831.

The Treatment of Addison's Disease by Whole Adrenal Gland

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ABSTRACT.—By cooling fresh suprarenal gland tissue immediately on removal from the animal, and by defatting, and mincing the same at low temperatures, and drying at 37°C. with the least loss of time, a preparation is obtained which in daily doses of 3 grm. per os, is effective in restoring a large measure of health to sufferers from Addison's disease.

It is essential that a potent extract of suprarenal cortex be available for (*a*) restoring the patient sufficiently to enable whole gland treatment to be instituted and (*b*) to treat any return of abdominal symptoms or circulatory collapse induced by intercurrent illness or failure to retain the whole gland through vomiting.

[1] Dr. A. C. Crooke and Dr. D. Russell, in a paper to appear in the *Journal of Pathology*, state that the number of basophil cells in the anterior lobe of the pituitary gland is reduced to from 1/50th to 1/500th of the normal in cases of Addison's disease.

It is desirable to increase the intake of sodium chloride to 10 to 15 grm. daily.

Neither saline alone, nor cortical extract alone produces the same effective result as whole suprarenal gland prepared as above administered per os.

Commercial preparations of whole suprarenal can be entirely without effect.

Subcutaneous injection of adrenalin in a phase of weakness may have disastrous results.

Trials, using the whole gland preparation on normal subjects, further establish the observations of Rowntree, that the gastric musculature is stimulated by injection of whole suprarenal gland. In certain cases, considerable elevation of blood-pressure may also result.

RÉSUMÉ.—Le traitement suivant des glandes surrénales fraiches donne une préparation capable, en doses de 3 grammes par jour, par la bouche, de rendre une grande mesure de santé aux malades souffrants de la maladie d'Addison. Le tissu surrénal frais est refroidi immédiatement après son excision de l'animal, la graisse est enlevée, le tissu haché à une température basse, et desseché à 37°, aussi rapidement que possible.

Il est essentiel d'avoir à sa disposition un extrait cortico-surrénal efficace (*a*) pour remonter le malade suffisamment pour rendre possible le traitement par la glande totale, et (*b*) pour traiter les récidives des symptomes abdominaux ou le collapsus circulatoire dus à une maladie intercurrente ou aux vomissements qui ne permettent pas de retenir glande totale dessechée.

Il est utile d'augmenter l'ingestion de sel à 10-15 grammes par jour.

Ni le sel ni l'extrait cortical seul ne produit le même effet que la glande surrénale totale préparée de la manière décrite ci-dessus, administrée par la bouche.

Les préparations de surrénale totale du commerce peuvent être absolument inefficaces.

L'injection d'adrénaline pendant un état de faiblesse peut avoir des résultats désastreux.

L'administration expérimentale d'une préparation de glande totale à des sujets normaux a confirmé l'observation de Rowntree que les muscles de l'estomac sont stimulés par l'injection d'extraits de glande totale. Dans certains cas il résulte aussi une élévation considérable de la pression sanguine.

ZUSAMMENFASSUNG. — Durch Kühlen von frischen Nebennieren sofort nach der Entfernung vom Tier, Entfettung, Zerschneiden bei niedriger Temperatur und möglichst raschem Trocknen bei 37°, bekommt man ein Präparat welches geeignet ist, in Dosen von 3 g pro Tag, peroral, die Gesundheit von Addisonkranken weitgehend zu bessern.

Es ist unbedingt notwendig dass ein wirksames Nebennierenrindenextrakt zur Verfügung stehe (*a*) um den Zustand des Kranken so zu bessern dass die Totaldrüsenbehandlung eingesetzt werden kann, und (*b*) für die Behandlung etwaiger Rezidiven der Abdominal-beschwerden oder eines durch interkurrente Krankheiten verursachten Kreislaufskollapses, oder das Erbrechen des Totaldrüsenpräparates.

Es ist wünschbar die Kochsalzzufuhr auf 10-15 g täglich zu erhöhen.

Weder mit Salz noch mit Rindenextrakt allein können dieselben Erfolge erzielt werden als mit dem oben beschriebenen Präparat der ganzen Nebenniere.

Die Handelspräparate von ganzer Nebenniere sind oft ganz Wirkungslos.

Die Subkutaneinspritzung von Adrenalin bei einem schwachen Zustand kann sehr schädlich wirken.

Versuche mit Totaldrüsenpräparat bei Gesunden haben die Beobachtung Rowntrees weiter bestätigt, dass die Magenmuskulatur durch Einspritzung eines Totaldrüsenpräparates gereizt wird. Bei manchen Fällen kann auch eine wesentliche Blutdruckerhöhung erfolgen.

THE cases which provided the basis for this therapeutic investigation here reported, were seen in private practice in Adelaide, South Australia, by Dr. C. T. C. de Crespigny and Dr. A. F. Goode, M.B., B.S., respectively. The former has, with one of us (C. S. H.) given a clinical account (from which the case notes here given are taken) before the Australian Association of Physicians, before whom Case I was demonstrated. Having in mind the reported tendency of Addison's disease to spontaneous cure or remission, the facts are presented at this stage (for investigation is still going on) in order that other workers may apply them with a view to establishing the truth more expeditiously; and to allow of possible cure of otherwise hopeless cases.

Case I.—C. H. An electrician. First seen in January 1930, when aged 28. He then complained of vague feelings of lassitude and weakness, and said that on a recent occasion

he nearly fainted while at the lavatory. His past history, heredity, and habits were without significance. On examination he was seen to be a lean, rather pale young man, weighing 146 lb. There were no abnormal physical signs. The urine was normal and the blood-pressure 80/116.

Nothing noteworthy occurred in his medical history during the next three and a half years. He increased in weight and remained well, except for trivial ailments, until October 1933.

Then he began to experience increasing fatigue at work, and became more and more dizzy on climbing stairs, stooping, or exerting himself in any way, but while sitting or lying quite still he felt well.

On December 27, 1933, he felt faint during breakfast and had to lie down. From this time he was unable to stand because if he did he would "go off in a faint." He vomited frequently every day at this time.

On January 5, 1934, he was brought to hospital in Adelaide. On examination, he appeared pale and his voice was rather feeble. His pulse was regular; 92. Blood-pressure
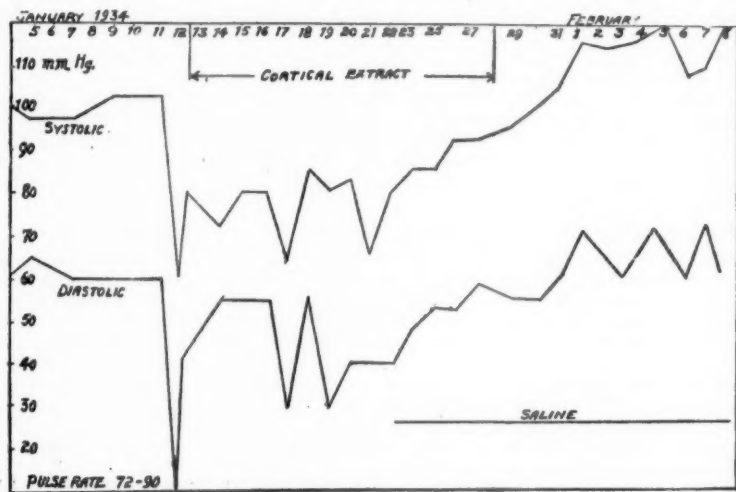
C. H. Blood-pressure chart.

62/100. There were no organic signs of disease and the urine was normal (limpid, acid, specific gravity = 1020, no albumin or sugar).

His reaction to standing up was as follows: He became extremely pale, his pupils dilated, and the lips became livid. His pulse became almost imperceptible. These symptoms were immediate and increased rapidly so that he would have fallen if not supported. He was in the erect posture for about thirty seconds. On lying down again his pulse had not increased above 96, but his blood-pressure had fallen from 64/104 before the experiment to a systolic pressure of 85 mm. Hg. The diastolic pressure could not be measured.

During the next few days his state remained the same. He slept fairly well with the aid of 5 gr. of barbitone. During his waking period he was very restless, tossing his limbs about and sighing like a person who has recently lost much blood. Sudden vomiting occurred sometimes unrelated to food. The daily amount of urine was from 30 to 45 oz. The bowels acted daily.

On January 12 he vomited about 2 oz. of greenish fluid at 2 a.m. and again at 7 a.m. Immediately afterwards he collapsed. The pulse was almost impalpable and the respiration sighing. He was very restless. The pulse was 100 and regular. He was cyanosed and unable

to speak. He remained in this state, with little change, for some hours. He complained of numb feelings in the arms. After a while he became irrational and more restless.

At 9 a.m. the systolic blood-pressure was 95; the diastolic could not be measured; the pulse was 100. The bed was elevated at the foot, and at 10 a.m. the systolic pressure was 105.

At 10.55 a.m. cortex extract (2 c.c.) was given by injection into the median basilic vein. Within a few seconds his condition became alarming. His face became deathly pale, the pupils dilated, and the pulse almost disappeared but did not increase in rate. The respirations were very shallow, and consciousness was lost. This condition lasted for some three or four minutes, after which he began to revive.

At 2 p.m. he complained of abdominal pain. His temperature was then 100° F.

At 9 p.m. another severe collapse occurred. 10 c.c. of cortex extract were injected into the glutei, and he gradually improved throughout the night.

The next day (January 13) his temperature was 100·8° at 8 a.m. Pulse 128 and respirations 20 per minute. The systolic blood-pressure was at 9.30 a.m. 60 mm. Hg, when 10 c.c. of cortex extract was injected. At 2.15 p.m. the blood-pressure was 40/80, and at 8.15 p.m. 40/90.

During the next few days he remained in a critical state, but with gradual improvement. He received from 5 to 10 c.c. of extract every day with two or three exceptions. The pulse-rate varied from 88 to 100, the blood-pressure from 30/65 to 55/90, the daily volume of urine from 18 to 42 oz. Nausea and vomiting were constant and exhausting. On January 15 he vomited 40 oz. of fluid and took only 26 oz. After this the amount of vomitus was rather less. His mind was unclouded, but his exhaustion was intense, and he was unable to be lowered to the horizontal position.

During this time he was given ephedrine gr. ⅓ 4-hourly, January 13 to 16 and subsequently adrenalin 30 min. 4-hourly by the mouth. Neither seemed to produce any immediate result.

January 22: Cortex extract 2 c.c. with adrenalin 0·12 c.c. was given intramuscularly. Adrenalin was subsequently discontinued, and uzara 5 gr. t.i.d. substituted.

January 23: Normal saline solution (sodium chloride, 1 drachm to a pint of water) was begun; 32 oz. were given this day. Subsequently this was continued. From 2 to 4 pints were administered daily. The saline solution was taken quite readily.

During the next few days the vomiting gradually lessened, and finally occurred only at long intervals, while the patient's general state greatly improved. On January 29, for the first time, vomiting was absent.

He was receiving cortical extract 8 c.c. daily during this period.

February 2 : On this day the bed was horizontal, and the patient was wheeled outside. He was cheerful and ate with a good appetite. Temperature 96·8° F. Pulse 80. Respirations 20. Urine 66 oz.; fluids taken in twenty-four hours: 89 oz. including normal saline 42 oz.

February 4 : Cortex extract 1 c.c. injected and 8 tablets of special B.W. whole gland preparation given orally.

February 5 : Patient vomited; cortex extract 8 c.c. was injected intramuscularly. This was repeated daily.

February 9 : The patient was raised to a sitting posture but the pulse became very feeble and the systolic blood-pressure could not be registered. The patient looked as if he were dying but soon revived on lying down again.

February 12 : Whole gland tablets 20 daily were given before breakfast with cortin 1 c.c. intramuscularly.

February 15 : Thirty whole gland tablets daily. Intramuscular injection discontinued.

The patient gradually increased in strength so that he was able to sit up, then to stand, and finally to go for walks without discomfort. He ate well, slept well, and had no gastro-intestinal symptoms. He was discharged on March 23 taking 30 tablets daily and about 2 to 3 pints of normal saline. Sphygmobologram = 75% of normal.

In April, patient resumed his duties as an electrical engineer with the Broken Hill Proprietary Smelters at Port Pirie.

Relapse.—Early in May he had an attack of mild respiratory catarrh. At once he became restless—constantly tossing his limbs about. His colour was "earthy." Nausea was constant, and vomiting frequent, so that he was unable to retain the gland tablets.

He was admitted to hospital on the second day. Cortical extract was injected intra-muscularly, 6 c.c. daily.

On the third night after the attack had begun he was delirious and tried to get out of bed several times; but the next day he rapidly improved and was able to go home on the eighteenth day.

The blood-pressure was lowest on the fifth day when the temperature was 103°.

Supplies of gland are now sent to him monthly. He cycles daily 5 miles to his work, and in November 1934 described himself as "fitter than ever."

A study of blood-pressure changes throughout the twenty-four hours over a period of six weeks proved conclusively that the height of the blood-pressure was closely related to the intake of whole gland, and that the best results were obtained when the dose was divided into four parts given at 8 a.m., 12 noon, 6 p.m., and 9 to 10 p.m.

Special examinations made throughout course of illness.—Skiagrams of lungs and heart showed nothing abnormal; skiagrams of suprarenal regions showed no evidence of calcification.

Fasting blood-sugar, 12.1.34 was 0·115%.

20.6.34 : Fractional test meal : stomach empty in one and a quarter hours ; no free hydrochloric acid in any specimen.

The electrocardiogram was normal when patient left hospital, and there was no alteration of the T-wave after the climbing of stairs. Ergometer (27.6.34): Right, 85 ; left, 65. Basal metabolic rate normal.

Attempts to estimate glucose tolerance were defeated by vomiting.

Pigmentation : There was none when patient was seen at the beginning of 1932. During his illness definite brownish pigmentation was present on the face, mainly at the sides and upon the neck. The backs of the hands and forearms were also pigmented and upon the forearms were scattered numerous darkly pigmented moles. The patient said that these had become visible only lately, and that they were becoming darker and more numerous. The areolæ of the nipples were not particularly brown.

The buccal mucous membrane showed pigment in the gums adjoining the upper and lower incisors, but the mucous membrane of the cheeks and palate showed no pigmentation.

Since treatment the pigment has completely faded and the dark line on the gums has almost disappeared (May 31, 1934), the patient's complexion being described as sallow, but with definite capillary coloration over the cheek-bones.

During February the patient demonstrated that he could brush off from his arm on to the bedclothes the dark pigmented spots which had developed during the illness.

Case II.—A. M. P., aged 41, architect ; actively athletic, good tennis and golf player ; highly-strung, introspective type. History of occasional severe abdominal (umbilical) "cramp," dating from an attack of pneumonia on service in 1918. Otherwise nothing relevant. Bronzing first noticed towards end of summer 1934 and mistaken for sunburn. When, however, patient found it necessary to rest all Sunday following Saturday's tennis, his physician diagnosed the true nature of the bronze pigmentation. Thus this case provides the reverse order of appearance of characteristic symptoms to that in Case I, in which faintness following exertion was a severe symptom before the pigmentation developed.

As in the previous case, recourse was made to cortical extract to combat abdominal crises and circulatory collapse, though it appears that the severity of the former vastly outweighed the latter in this instance.

About 10.7.34 an attempt was made to replace injections by orally administered whole gland. Progress was so rapid, and improvement so great that the patient (who never was as prostrate as the patient in Case I) played golf, and did some gardening. This was on 21.7.34 at which date 3 grm. of gland were being administered without cortin. Salt intake had been raised to 10 grm. daily.

The patient, unlike the patient in Case I, showed a tendency to develop abdominal crises, one recurring without warning on 24.7.34. It was completely relieved within ten minutes, the effect beginning immediately. The cause seems to have been over-exertion at golf, etc. After this, 1 c.c. of extract was given daily, together with 3 grm. of gland but the patient did not recover his usual vigour. Predominating symptoms were, lack of appetite, "indigestion," poor sleep, and a return of giddiness on exertion. Finally, to shave himself came to require an effort. By 12.8.34 abdominal spasms appeared and were relieved by injection of 1 c.c. of extract. But depression and the tendency to vomit and signs of abdominal discomfort persisted until 10.30 a.m., 17.8.34, when vomiting became urgent and abdominal pain excessive ; 1 c.c. of extract was only partially effective after twenty minutes.

Blood-pressure was about 80 mm. systolic. The administration of whole gland was stopped, and by 6 p.m. systolic blood-pressure = 100 mm. and complete relief was experienced by 8 p.m.

From this point onwards whole gland was replaced by 2 c.c. of extract night and morning. Relief was "indescribable." During the ensuing four weeks on this treatment the patient slept well and the systolic blood-pressure remained at 100 mm. Although there were no signs of abdominal disturbance the patient found that he became readily exhausted by effort, and always noticed a vague abdominal discomfort and giddiness when he had even slightly overtaxed his strength, which was, of course, very limited. It was decided to re-establish the whole gland treatment, beginning with 6 and rising to 17 tablets daily. By 15.9.34 on 2 c.c. extract + 2·5 grm. tablets daily patient felt much improved, notably in respect of reaction to effort, and by 16.9.34 could weed his garden without giddiness, although that symptom returned on 19.9.34 when the dosage of whole gland had reached 3 grm. daily.

The dose was distributed throughout the day and by dropping the last dose of 0·5 grm. at supper, a better result was obtained. Total dose 2·5 grm.

From 18.9.34 patient returned to his office duties and by 13.10.34 felt fairly well, but there was a tendency to indigestion and a feeling of "pins-and-needles" every night after dinner for three hours. Stayed at home 23.10.34 quite ill. Stomach upset. On 24.10.34, 3 c.c. of extract were administered at intervals, the blood-pressure being 90 mm. systolic. After three days of three injections each whole gland, being taken simultaneously, the patient felt well again and returned to office. No indigestion and no "pins-and-needles" after food; feeling confident (30.10.34).

From this point onwards there was a steady gain in feeling of well-being, and a better knowledge of exactly how much energy to give out. Patient's colour became almost normal and on 30.11.34 pigmentation had almost disappeared from the gums. The weight has remained constant at 11st. 3lb.

In both these cases the patients manifested complete inability to read a novel, owing to the impossibility of concentrating attention, and the first reading done by the patient in Case I was after two months' treatment, when he could at first only manage the newspaper. This patient, moreover, although he was cheerful and able to coöperate quite intelligently during the first six weeks of his severe illness, has remembered nothing of what happened during that period.

Treatment.—The potent cortical extract prepared by the method of Grollmann and Firor [4] made it possible to restore the patients in these two cases sufficiently to proceed further with therapeutic investigation. The salt intake was increased by 15 grm. daily, following the work of Harrop and his colleagues [6]. Vitamin C intake was also increased. It became evident that we could not continue with cortical extract, which was costing too much to be of practical value to the patients. Moreover, though the severe symptoms had been suppressed, recovery of normal physical capacity appeared to be unlikely. An attempt to replace the injections by giving adrenal gland (whole) tablets, was followed by collapse within twelve hours. This attempt was nothing more than a repetition of Muirhead's method [9].

From the blood-pressure chart in Case I (p. 64) it will be seen that under the influence of cortical extract, recovery from the condition of "shock," insisted upon by Harrop [7] as being the true state of affairs, was associated with only a slight rise of blood-pressure which, however, improved steadily from the point at which saline intake began. Dilute hydrochloric acid greatly improved digestion and desire for food.

There appear to be three stages of response to therapy. (1) By means of cortical extract the abdominal symptoms and vomiting and extreme low blood-pressures are favourably influenced. The vascular recovery at this stage is, however, more of partial recovery of some capacity for dealing with changes of vascular loading. (2) Increased salt intake, by increasing that water content of the body, and especially of the blood, improves the blood-pressure by 50% (in these cases, when cortical extract is given). See, however, Harrop and his colleagues [7] for a contrary view

of the action of "cortin." (3) Whole suprarenal gland suitably prepared, in doses of 3 grm. given by mouth, improves both the subjective feelings of physical well-being and desire for effort and the capacity for effort. This occurs in the absence of cortical extract. Daily variations in blood-pressure follow the infection of the gland so closely as to require the administration to be spread over the whole twenty-four hours. (4) Whole gland as found in commerce, has no effect on the syndrome. (5) Adrenalin, ephedrin and uzara, had no effect on the gastric symptoms (cf. Muirhead and also Rowntree) which invariably respond to administration of cortical extract. (6) There is sufficient difference both between the qualitative nature of the syndromes, and the therapeutic response obtained in the two cases, to confirm the opinion that the term Addison's disease is a wide one covering a range of types of "adrenal insufficiency," which advances in therapy will enable us to differentiate. These summarized conclusions must be taken to apply only within the limits of experience of these two cases.

Untoward results of therapy.—It was found that if taken either in a large dose, or in small doses on an empty stomach, the whole gland preparation produced a sense of ill-being ranging from a mere suggestion to severe pain and vomiting (cf. Rowntree). These effects were obviated by distributing the dose throughout the day, giving it after food, reducing it to the lowest compatible with therapeutic efficiency, and where necessary (*see* Case II) temporarily withdrawing the preparation, and using cortical extract intramuscularly to prevent—or cure—an obvious return of gastric disturbance, however occasioned.

Adrenalin was injected (2 minims, 1 : 1,000) subcutaneously during a period of prostration on 13.1.34 (Case I) when cortical extract was being administered. It was a very hot day, and the patient was acting just as though he had lost much blood, possibly because of the demand for increased cutaneous supply. The systolic blood-pressure was approximately 74 mm. Our object was to test the vascular response, and to test Muirhead's observations. The effect was both immediate and alarming. The pulse disappeared except in the carotids. The pupils dilated, and consciousness was lost. The pulse-rate remained unaltered and was counted until the patient recovered, the systolic pressure rising finally to 108 mm. in four minutes.

Since only a very minute amount of the injected adrenalin could have reached the circulation in the first moment following injection, the effect must have been due, either to the presence of some oxidation-product of adrenalin—to which in the circumstances the subject was sensitive, or to vasodilatation caused by the access of minute amounts of adrenalin. That such possibilities exist is shown by the work of Dale [3], Gruber [5] and, recently, Rein [10]. That the vagus was not involve is proved by the unchanged cardiac rate, and that the effect was not due to cardiac overloading from widespread vasoconstriction is shown by both the unchanged rate and the rapidity of the response. On the other hand, the very fact of the unchanged rate, points to the temporarily complete loss of reflex response to vascular loading in the circumstances. This experience with adrenalin is important, as its use is advocated both by Muirhead [9] and Rowntree [11] as a therapeutic measure.

A five-day trial with twelve medical-student volunteers, taking 3 grm. of whole gland, gave the following results. Blood-pressure rise of 10 mm. and over, in five cases ; blood-pressure fall of 5 to 10 mm. in one case, proved to be a case of anterior pituitary dystrophy; this was associated with violent gastro-intestinal disturbance, vomiting and prostration. About 30 minutes after taking the tablets, all the subjects experienced gastric-disturbance, ranging from a very slight degree to one relatively severe, with vomiting, when the tablets were taken on an empty stomach. (cf. Rowntree [11A]).

One case of obscure muscular dystrophy of thirty-five years' standing showed a rise of systolic blood-pressure of 35 mm. after two days, and 45 mm. after eight days'

administration of 3 grm. daily, and maintained this elevated pressure until cessation of treatment, when the blood-pressure fell to normal in twenty-four hours. There were no gastric symptoms whatever. Large doses of adrenalin given by mouth did not affect the blood-pressure, or cause any symptoms.

Preparation of whole gland.—Immediately on removal from the oxen, the glands were placed on ice, and transported rapidly thereafter to the Biochemical Laboratory, placed in a refrigerator, and cooled below zero (about $-4°$ C.). They were defatted manually while cold, as rapidly as possible, and minced at zero, as soon as practicable after the death of the animals. The minced gland was then spread out in a serum-drier, and rapidly dried at $37°$ C. (about three hours). It was tableted for dosage purposes, but the tablets were broken before use and mixed with jam, which was found to be a good medium to aid ingestion of the rather pungent-smelling material. It was found to keep apparently unimpaired, at ordinary temperatures, in a bottle, for at least 4 weeks. The main supply has been kept at $-4°$ C.

The first recorded case of the use of whole gland in Addison's disease is by Lloyd-Jones, 1895 [8], but an error of diagnosis was believed to explain the improvement found, as the patient died of pernicious anæmia. Bramwell 1897 [1] injected sterile suprarenal juice, and appears to have had good results, for a post-mortem examination (after death from influenza), disclosed atrophied adrenals. Stockton 1898 [14] also reports good results from the eating of fresh suprarenal tissue. Adams, 1900, reported a case of Fraenkel's in which the patient survived at least $8\frac{1}{2}$ years after suprarenal feeding but in which the cure had been considered to be spontaneous. Simpson 1931 [13] used a Swingle-and-Pfiffner cortical extract which was much less potent than that used in these cases, and found that desiccated adrenal gland, given by mouth, was effective in maintaining the ground gained by the use of the extract. Charpentier 1933 [2] reported, rather incompletely, some degree of success from Muirhead's treatment. Muirhead [9] used too little gland to be of any use, so far as our experience can take us, and, from the results of commercial whole gland, it would appear that conflicting reports may be due to (1) the destruction—either by mode of preparation or on keeping—of active principles in the tissue, or (2) wide variations in the degree of involvement of several factors going to make up the syndrome. We cannot agree with Harrop, Weinstein, and Soper [6] that cortical extract does not affect the blood-pressure or the pigmentation, although one estimation of blood-pressure in a crisis does corroborate their contention that loss of fluid from the blood-stream is involved. The papers of Harrop and his colleagues, and of Rowntree, should be consulted for a complete review of the results of modern therapy, and of post-mortem findings in Addison's disease.

BIBLIOGRAPHY

1 BRAMWELL, *Brit. Med. Journ.*, 1897, i, 1, 67.
2 CHARPENTIER, *Lancet*, 1933 (ii), 921.
3 DALE and RICHARDS, *Journ. Physiol.*, 1927, lxiii, 201.
4 GROLLMANN and FIROR, *Journ. Biol. Chem.*, 1933, c, 429.
5 GRUBER, *Amer. Journ. Physiol.*, 1928, lxxxiv, 345.
6 HARROP, WEINSTEIN, SOPER and TRESCHER, *Journ. Amer. Med. Assoc.*, 1933, c. 1850.
7 HARROP and WEINSTEIN, *Journ. Exp. Med.*, 1933, lvii, 305, *et seq.*
8 LLOYD-JONES, *Brit. Med. Journ.*, 1895 (ii), 483.
9 MUIRHEAD, *Journ. Amer. Med. Assoc.*, 1921, lxxvi, 652.
10 REIN, *Klin. Wchnschr.*, 1930, ix, 1485; and *Zeitschr. f. Biol.*, 1930, xci, 13.
11 ROWNTREE, *Journ. Amer. Med. Assoc.*, 1922, lxxix, 556.
11A Id., *ibid.*, 1925, lxxxiv, 327.
12 ROWNTREE, GREENE, SWINGLE and PFIFFNER, *ibid.*, 1931, xcvi, 231.
13 SIMPSON, *Proc. Roy. Soc. Med.*, 1931, xxiv, 497 (Clin. Sect. 51).
14 STOCKTON, *Med. News*, 1895, lxvii, 551.

Dr. S. LEVY SIMPSON said that Professor Hicks' observations were significant in suggesting that a crude preparation of adrenal cortex contained additional factors to those present in the more purified extract that was used for parenteral injection.   Some experiments on adrenalectomized rats (*Journ. Path. and Bact.*, 1934, xxxix, 569) that he (the speaker) had carried out in collaboration with Professor Korenchevsky and Dr. Dennison, at the Lister Institute, had shown that injections of cortical extract, although maintaining life, did not produce or maintain complete normality in the absence of regeneration of the animal's own adrenal or accessory adrenal.   His own clinical experience tended in the same direction and raised the question as to whether the cortical extract injected contained all the essential factors. Rogoff had used a relatively crude extract by mouth for some years and some of the material which he had kindly sent to him (Dr. Levy Simpson) had proved beneficial in one case of Addison's disease of moderate severity. (*Proc. Roy. Soc. Med.*, 1934, xxvii, 28). He believed that the abdominal pain produced by some extracts of adrenal gland taken by mouth (and to which Professor Hicks referred) was due to adrenalin.   Similar pain was caused by 1 c.c. of 1 : 1,000 adrenalin solution by mouth and in collaboration with Dr. G. Vilvandré, he had found (*Proc. Roy. Soc. Med.*, 1934, xxvii, 21) that this was associated with active jejunal contractions.

Although whole gland given by mouth, or adrenalin, or sodium chloride, might have their place in the therapy of Addison's disease, the most reliable measure at present in a real crisis was parenteral injection of a relatively pure cortical extract.

[*The report of other papers read at this meeting will appear in the next issue of the* PROCEEDINGS *of the Section.*]

Section of Comparative Medicine

President—J. B. BUXTON, F.R.C.V.S.

[*February 27, 1935*]

DISCUSSION ON INFLUENZA IN MAN AND ANIMALS

Dr. C. H. Andrewes: It is difficult to decide exactly what influenza in man is; still less what is meant by influenza in animals. Probably the term influenza is used in human medicine with two distinct meanings. First, in its narrower sense, there is epidemic influenza which periodically attacks this country with greater or less severity; my co-workers, Drs. Laidlaw and Smith, and I believe that this disease is caused primarily by a virus which will infect ferrets and mice [1]. Secondly, there is human influenza in a much wider sense. Influenza figures in the death returns in almost every month of every year, and it is diagnosed every winter in the absence of an epidemic. It is sometimes merely a convenient label for upper respiratory infections of unknown ætiology. Possibly it includes a number of disorders; at any rate we have obtained as yet no evidence that a virus capable of infecting ferrets is present in sporadic cases of influenza in this wider sense.

The definition of influenza in animals is still more difficult. Swine influenza is a well-known disease in the middle west of the United States and has been recognized also in Germany and France. It has a very good claim to the title influenza, for it is caused by the combined action of two organisms, one a virus closely related to that isolated by us from cases of human influenza, the other, a bacillus, *Hæmophilus influenzæ suis*, which is a variety of Pfeiffer's bacillus [2].

The use of the term influenza in a disease of horses is sanctioned by custom. There is as yet no evidence that the ætiological agent is related to those of human and swine influenza. If, nevertheless, we continue to use the term " horse influenza " we must realize that, so far as we yet know, the disease is no more allied to human influenza than is swine erysipelas to human erysipelas.

But it seems desirable to draw the line at this point and to abjure the use of the word " influenza " in animal diseases unless and until such diseases are shown to be related to influenza of man and the pig (and perhaps the horse). There are many upper respiratory diseases of animals and birds, but to apply the word influenza to them without real justification is, I submit, only to confuse further a sufficiently complicated subject.

I will now turn to experimental influenza in the ferret and mouse. The symptoms produced by our human and swine strains in ferrets and mice are identical; the two can be certainly distinguished in these animals only by immunological tests. Antigenically they are different but not completely so; titrations show that antisera to the two strains have a definite overlap.

Either strain [1] infects a ferret, but only when inoculated intranasally, or directly into the lung; introduction of the virus subcutaneously, intracerebrally, or by any other routes, produces no disease. Infected ferrets show a rise of temperature in forty-eight hours; often this drops and rises again after a further

forty-eight hours, giving a biphasic curve. They develop nasal catarrh and obstruction and sneeze repeatedly. After a few days their fever and local symptoms abate; they recover and for some months are immune to reinfection. Just as we can infect only by the respiratory tract, so we can recover virus only from the ferret's nasal passages and lungs; we have not found it elsewhere. Suspensions of infected turbinates or lungs can be used to carry the virus on in series and we have thus transmitted it through more than a hundred passages. If the ferrets are infected while under ether anæsthesia, they develop widespread pulmonary lesions. Affected lobes or parts of lobes are plum-coloured and airless and show, histologically, œdema and bronchopneumonia. Often they are sterile on cultivation, but sometimes bacteria may be grown, no one organism being present with any constancy. This lung involvement in ferrets inoculated under anæsthesia was first shown by Shope [3] to be produced by the swine influenza virus, but Francis [4] in America and we ourselves have found the same to be true of human strains: lung-involvement may prove fatal.

An advance was made last summer when we found [5] that mice were susceptible to the virus when this was introduced intranasally under ether anæsthesia. In contrast to ferrets, mice do not appear to develop symptoms or lesions in the nasal passages, but only in the lungs. These consist of areas of plum-coloured consolidation which may be very limited in extent or in fatal cases may involve the whole of the lungs. Histologically they are like the ferret lungs, showing congestion, collapse, œdema, and infiltration with polymorphonuclear and mononuclear cells. Bacteriologically also they are like the ferret lesions—often sterile, but at times there are various secondary invaders. Mice infected with potent virus usually show symptoms—roughening of the coat, exaggerated respiration and loss of appetite—in about forty-eight hours and they usually die within a week. Mice receiving smaller doses of virus commonly survive. As with ferrets, we have so far only recovered virus from the respiratory tract; lung emulsions can conveniently be used for carrying on the virus serially through mice.

One important point has to be emphasized. Bacteria-free filtrates of virus are adequate to produce the whole disease-picture in both ferrets and mice. No association with a bacillus is necessary. Nor indeed have we yet found any organism which when associated with virus profoundly alters the disease-picture. Here, then, is a striking contrast with the disease in pigs [2] where the virus alone produces a mild, scarcely recognizable illness and the typical " swine 'flu " is only seen when both virus and influenza bacillus have been introduced. As to what is necessary to produce influenza in man, we do not know. We cannot say whether Pfeiffer's bacillus plays an important accessory role or not in uncomplicated influenza. We feel fairly sure, however, that in killing epidemics like that of 1918-1919 associated bacilli and cocci play a very important part indeed.

During the past autumn Dr. Thomas Francis [4], in New York, obtained sputa sent in glycerin from cases of influenza in an outbreak in Porto Rico. With these he was able to infect ferrets and from the ferrets to infect mice. Essentially his results confirm ours, but some of his strains seem to be even more virulent for animals.

I will refer to some of our observations upon immunity to influenza. Ferrets recovered from an infection are immune for some three months. Thereafter their immunity fades, and six months after their first attack they can be reinfected. After an attack of the disease they develop neutralizing antibodies in their sera, and at the time when their immunity has faded and they are again susceptible, these antibodies are still present. We do not know whether the ferrets have become susceptible because their antibodies are now quantitatively insufficient or whether we shall have to make some distinction between local and general immunity. In the same connexion it may be recorded that subcutaneous immunization of ferrets with

living virus has, so far, failed to give them complete protection against infection; it does, however, lead to the development of neutralizing antibodies in their sera: here again is an apparent instance of divorce between humoral immunity and susceptibility to infection.

Almost all the human sera we have examined contain neutralizing antibodies against the virus. It seems very unlikely that all these people will prove resistant to the next epidemic which comes along. If they are not, why not? Will it be because their antibodies are not strong enough, or because humoral immunity is of no account? Or will the virus of the next epidemic be of a different antigenic race?

We should be very rash to claim, at this early stage, that " a true influenza " of man can be distinguished from " pseudo-influenzas " by determining the presence or absence of a virus pathogenic for mice and ferrets. It may be that even in sporadic influenzas in non-epidemic times a virus is present but that it is insufficiently potent to infect our animals. We feel, however, that the animal test places in the hands of investigators a new tool with which to attempt the sorting-out of this complicated group of diseases.

REFERENCES

1 SMITH, WILSON, ANDREWES, C. H., and LAIDLAW, P. P. *Lancet*, 1933 (ii), 66.
2 SHOPE, R. E. *Journ. Exp. Med.*, 1931, liv, 373.
3 Id., *ib.*, 1934, lx, 49.
4 FRANCIS, T., jr. *Science*, 1934, lxxx, 457.
5 ANDREWES, C. H., LAIDLAW P. P., and SMITH, WILSON. *Lancet*, 1934 (ii), 859.

Dr. J. T. Edwards : It may be judged from Dr. Andrewes' remarks that research into influenza has at last taken shape as a problem in comparative pathology. It is thus fitting that the progress of research on this subject should be discussed by this Section. Let me, therefore, in making the point I wish to bring out in my contribution, retrace some of the ground which has already been covered by Dr. Andrewes.

It can be looked upon as fortunate that the ferret (which had been discovered by Dr. Andrewes' colleagues at Hampstead—Laidlaw and Dunkin—to be invaluable in their researches upon distemper in dogs) was found to be susceptible to the virus of human influenza, when it is inoculated by the intranasal route with the nasal washings of persons suffering from influenza. As has been said, the lesions of the ferret disease disclose no bacteria as likely causal agents; the disease is readily transmissible by means of filtrates: much has been learned about its immunological characteristics in the ferret (a subject I shall revert to later), but, so far, the natural host, namely man, of what is presumed to be the virus thus transmitted to the ferret has not been infected with material derived from the ferret disease. The further finding that the mouse can be infected with the ferret virus by intranasal inoculation, with the production of characteristic lung lesions, may well furnish the means of ready and economical quantitative estimation of virus in tissue material, and thus help to speed up investigation, after the manner in which the mouse and guinea-pig, respectively, have been used in research on louping-ill and foot-and mouth disease.

I submit, however, that this work might have reached an impasse, had it not been that concurrently a disease of pigs, well known in America since 1918 as swine influenza, was under investigation by Shope at the Rockefeller Institute ; Shope, with Lewis, in a number of papers since 1931, has shown that the pig disease is a composite infection, with, as its primary exciting agent, a filter-passing virus, which alone produces merely a mild disease (that is, however, readily transmissible by contact); symptoms corresponding in severity with those of the natural disease can only be set up when the virus acts in concert with a bacterium, *H. influenzæ suis.*

Shope's work, it must here be said, followed upon the discovery of the American veterinary workers, McBryde, Niles, and Moskey, in 1928, that: (1) The pig disease was an affection of the respiratory tract and the causal agent was not found in the blood; (2) the infective agent was readily demonstrable in the tracheal and bronchial mucus and in the nasal secretions of diseased pigs; (3) the disease could be readily transmitted by dropping suspensions of the tracheal and bronchial mucus or of the nasal secretions of affected pigs into the nostrils of healthy pigs, and in no other way.

I have found it necessary to repeat this much of the substance of Dr. Andrewes' remarks because, from a scrutiny of the relevant literature, it has been borne in upon me that the Great War and the circumstances arising out of it must now be adjudged to have delayed, probably for at least fifteen years, the course of research along these lines, which now bid well to be fruitful. Such work as has been taken up in the intervening period has consisted mainly of exercises in pure bacteriology, which on the whole have been barren of results that can be said to be likely to be applicable to the control of the disease.

Now, just before the war, that is, in 1912 and 1913, there was published in the *Zeitschrift für Veterinärkunde* a series of reports the significance of which was grasped only by a few men in veterinary circles at the time, although their general purport would seem to have been well appreciated by the men who sponsored or actively prosecuted the work and who bear most illustrious names in the realm of bacteriology, viz. Koch, Gaffky, Löffler. These reports dealt with a common respiratory disease of horses which had been causing regularly, especially during the colder months of the year, very heavy losses annually in the German army. This disease is well known to British veterinary surgeons as "equine infectious pneumonia" or "contagious pleuro-pneumonia," but, as has been stressed by the Dutch writer, Bemelmans (1921), it bears more points of resemblance to human influenza than does the other common form of equine infectious respiratory disease, the so-called "pink-eye" of British and American veterinary surgeons. "Pink-eye," however, is customarily referred to as influenza, following upon the subdivision by Falke, in 1862, in a notable treatise, of the more common respiratory diseases of the horse that had previously been massed together under the common designation of influenza.

The "pink-eye" form of infection (the *influenza catarrhalis* of Friedberger, *pferdestaupe, rotlaufseuche*) was quite well known to the German workers mentioned in the course of their investigations and was even investigated by them as a separate part of their inquiry. It is well known that this commonly designated influenza, often occurs in the form of extensive epizoötics which spread rapidly through stables and even large territories in a continuous wave. It can be readily transmitted from diseased to healthy horses by subcutaneous inoculation of blood. In 1909, Poëls, of Holland showed that it could be transmitted by a carrier stallion to mares during coitus. Mares infected in this way afterwards spread the disease rapidly by contact to healthy horses kept in the same stables, presumably by the respiratory route. Berkefeld fitrates of infective semen proved virulent on inoculation. In Poëls' case the stallion transmitted infection by coitus for a period of six years. In another case, recorded by Bergmann (1913) in Sweden, a stallion communicated infection in the same way for six years and a half. Vechiu (1926) in Roumania has shown that the virus can be found in the saliva of infected horses for at least eight months after apparent recovery. This form of disease is usually attended with only a low death-rate. After an incubation period of from two to twelve (usually four to seven) days, there is a sudden rise of temperature (104-106° F.), which lasts with fluctuations for from three to six days, and then drops rather suddenly. During the febrile period the horse shows marked prostration, muscular weakness, and incoördination of movements. The eyelids are swollen and the conjunctiva assumes a deep red to

mahogany colour. Œdematous swellings are often seen in the subcutaneous tissues of the lower part of the trunk and in the limbs. The amount of nasal discharge and cough varies considerably, but in what is usually held to be a typical case it is not large. It is, however, not always easy to distinguish this disease from the other form to be considered, of which inflammatory changes in the respiratory tract are the pronounced feature. In the extensive outbreak which swept across India in 1915, A. J. Williams records that in some localities, depending upon the general condition of the horses and other circumstances, the disease assumed a typical "pink-eye" or anasarcous form, whereas in other localities the symptoms were those of an acute catarrhal fever. In an epizoötic which raged throughout South Africa in 1916, Theiler was unable, after careful examination, to decide as to which of the recognized forms of influenza he was dealing with.

The equine infectious pneumonia (*influenza pectoralis* of Friedberger, *brustseuche*), which is the condition I wish to bring especially to notice, differs from the preceding condition mainly in that it comes to the notice of the practising clinician when the disease has reached the stage of a frank pneumonia or pleuropneumonia. It is also less rapid in its spread, which takes place by leaps, and the very high death-rate caused by it makes it a disease of formidable economic importance to horse-owners. It prevails only among horses kept in stables or otherwise in close confinement, especially during the colder weather, when working horses are usually stabled. The view has been expressed by competent veterinary authors that probably all cases of pneumonia in horses, including the apparently sporadic cases encountered by the clinician, are of this infectious type. The lung lesions differ from those of pneumococcus pneumonia in man in that they first make their appearance as widely scattered foci of mainly croupous inflammation in the lung parenchyma, which show a marked tendency to early necrosis followed by gangrene. In many cases there is enormous pleuritic effusion. Post mortem, one finds usually in pure culture, in the earlier foci in the lungs, the streptococcus (*Str. equi*) first described in these lesions by Schütz in 1887—a streptococcus which was for long afterwards believed to be the cause of the disease, but which does not differ from the kind usually cultivable from the submaxillary-gland abscesses of young horses affected with the common equine infectious disease known as strangles. The French veterinary worker, Lignières, however, ascribed both this disease and the form already considered to Pasteurella infection, that is, to a group of organisms that had previously been demonstrated in the lesions by Babes. There is a large continental literature upon the possible role of these two organisms in the causation of equine infectious pneumonia. It is interesting to recall that Pasteur in 1881 gave his attention to this disease. The horses belonging to the *Compagnie des Omnibus Parisiens* were suffering huge fatalities from it. Pasteur injected nasal discharge into guinea-pigs which afterwards died, and he obtained from various organs pure cultures of an ovoid bacillus which he thought closely resembled that of fowl cholera.

In spite of the considerable amount of work carried out to prove a causal relationship between the various cultivable micro-organisms and *brustseuche*, the disease could never be set up in horses artificially by these organisms, and all measures designed to protect horses by inoculation of any of the organisms or their products failed.

In 1900, therefore, the Prussian Ministry of War, alarmed by the heavy recurring losses caused by the disease, undertook official inquiries into its ætiology. The experiments were entrusted first to the distinguished veterinarians, Ostertag and Tröester, but the outcome of their work was that they failed altogether to discover what was the natural mode of transmission. Koch was then commissioned by imperial decree to pursue investigations into the matter at his institute in Berlin, with the coöperation of the military veterinary authorities. Like his predecessors

at the work, he concluded that all the cultivable bacteria, notably the streptococci, to be found in the lesions postmortem could be dismissed as secondary invaders or accidental contaminants. He noted, however, that in a few cases, which had run a hyperacute course, no bacteria could be discovered in the lungs. He also carried out careful experiments to ascertain whether other animals or vermin played any part as carriers or vectors of the infective agent. He was unable to incriminate such carriers, and his second report, written by Gaffky in 1911, concluded with the statement that the causation and mode of transmission of the so-called equine contagious pleuropneumonia remained an absolutely open question. After Koch's death (1910) Gaffky was commissioned to continue the researches at Koch's Institute, and the two further reports which were submitted to the Minister for War in September and December 1912, were published in the form of an article under the names of Gaffky and Lührs in the journal already referred to (*Zeitschrift für Veterinärkunde*, vol. xxv, pp. 1-11) in 1913. Having at their disposal a vast amount of animal material they were enabled to observe closely the pre-pneumonic clinical phase of the disease, i.e. what may be looked upon as the more typically influenzal phase, and to kill for inspection young horses exposed to infection by contact at any observed stage of the disease. The conclusions were as follows :—

(1) The initial lesion in the lungs is found in the smallest bronchi. At an early stage of the disease these passages are filled with a clear, yellowish, slimy exudate which readily coagulates, and in the vicinity of these collections of exudate there are areas in the lung of dense cell accumulation and serous infiltration. In the lobules communicating with the occluded bronchioles, the lung alveoli are also distended with fluid contents which are rich in extravasated cells. Where these foci underlie the pleura, there is œdema of the sub-endothelial tissue, which is filled with a transparent gelatinous exudate. There is also at the commencement of the disease a marked infiltration of the interstitial connective tissue with œdematous fluid.

(2) Next, about the fourth or fifth day after the onset of fever, bacterial invaders, particularly streptococci, make their appearance and then produce the severe croupous and often hæmorrhagic lesions which lead to widespread necrosis.

(3) Transmission as a rule takes place by contact from horse to horse without the intervention of vectors.

(4) The incubation stage is long—at least sixteen days ; it is usually between twenty and forty days, but may be even longer.

(5) The disease cannot be transmitted by parenteral inoculation of blood or diseased tissue pulp. On the other hand, transmission usually succeeds when the bacteria-free bronchial exudate which has been harvested during the early stages of the disease is rubbed into the undamaged surfaces of the nostrils and mouth.

The authors also write of the presence of bodies that bear some resemblance to inclusion bodies in the ciliated columnar cells of the affected respiratory mucosa.

The above conclusions would cover the work which had been accomplished until the end of 1912.

The issue of published reports then ceased and the work had to be discontinued abruptly with the declaration of war. During the war, and for some time afterwards, as Lührs has afterwards stated, the disease fell into relative insignificance because, as had been already observed in the German campaigns of 1866 and 1870-71, in the conditions of open-air field service, horses were remarkably free of the forms of respiratory disease which had previously afflicted them in the conditions of peace-time maintenance. Nevertheless, it must here be asserted that at remount depôts and collecting centres, and particularly in the conditions of sea transport, respiratory disease was often a serious menace to the horses of the belligerents.

It is to be hoped that the respiratory affections of the horse will prove amenable to study by methods similar to those which more recently have proved fruitful in investigating virus diseases. I have dealt with the subject here as it concerns

horses, not because of a desire at the present moment to press for an extension of the study to this species, but rather to bring to notice certain remarkable experiences in comparative pathology which seem to me to fit in very well with the picture as it has now been revealed by Dr. Andrewes. I would have hesitated, however, to make it the main theme of my contribution, had it not been that there has fallen into my hands a striking article written a few years ago by Gaffky's former colleague, Lührs (now a Veterinary-General in the German Army) recording what he had been able to salvage of the German records covering the period between the end of 1912 (when the last report was published by Gaffky and himself) and the outbreak of the war. This further report was not published until 1928, in a *Festschrift* dedicated to the distinguished veterinary teacher, Eugen Fröhner. Lührs tells in this report that the researches carried out at Koch's Institute under Gaffky were afterwards directed by Löffler, who deemed them to be of such great interest and significance that on his death-bed his concern was for them and their further extension. The further records are concerned with researches upon immunization against the equine infectious pleuro-pneumonia. In experiments that were several times repeated and seem to me to have been adequately controlled, it was shown again that when bronchial exudate, free from bacteria, taken from the lungs of young horses on the third or fourth day of their illness, was applied to the nostrils or mouth of susceptible horses, the latter almost invariably contracted the disease. In their protection experiments, suspensions of triturated lung lesions were employed. It had been found that suspensions prepared in this way did not set up recognizable disease when they were inoculated subcutaneously, intravenously, intrathoracically, or intramuscularly, but the inoculated animals subsequently resisted natural infection after they had been exposed to risk in every possible way. In view of these promising results, further work on a somewhat large scale was carried out, using for the experiments mainly lung material preserved in 50% glycerin : the animals inoculated with this material subsequently resisted infection by intranasal and intrabuccal rubbing of infective bronchial mucus, which almost invariably produced disease in the controls. It is mentioned that the period of incubation was shorter when the infective material was rubbed into the nostrils than when it was rubbed inside the mouth. The active agent would, therefore, seem to be unable to set up manifest disease except when it is brought into direct contact with the respiratory mucosa ; when it was intro-duced into the body by other channels it failed to set up overt disease, but was yet capable of evoking an immunity response of such degree that the inoculated animal was capable afterwards of putting up nearly always a solid resistance against natural infection.

While dealing with the subject of equine respiratory affections, mention has to be made of the recent work of Waldmann and Köbe upon a form of infectious bronchitis in horses which prevails seasonally in certain racing establishments in Germany and elsewhere, and which causes the affected animals to display paroxysms of coughing, with few other striking symptoms. The disease has been found by these workers to be readily transmissible among horses by contact, the incubation period being from two to three days. It could also be transmitted artificially by intranasal inoculation of bronchial mucus and lung expressate derived from horses killed at an early stage of the disease, when the lungs were still germ-free. Filtrates of suspensions of this material were also infective, and the disease produced was passaged twelve times in this way by filtrates. In severe cases, streptococci could be discovered in the peribronchial foci. Some immunity to reinfection was demonstrable, the degree of which seemed to correspond to the severity of the initial infection. The disease was also found to be transmissible to pigs and cattle. In cattle, the disease set up would appear to be identical with that seen in the small outbreaks of infectious bronchitis that have sometimes been reported

to occur naturally in these animals. The authors did not determine whether the pig infection which was brought about experimentally by them with the horse virus was identical with the form of pig influenza which they have had under study for some time in Germany, following upon the suggestive indications of Shope. The German form of pig influenza seems to exhibit certain well-marked points of difference from the American disease studied by Shope. It prevails as an extremely widespread winter enzöotic among pigs a few weeks old, in which formerly it was mistaken for chronic swine fever. It is manifested by great wasting and coughing, and it is noteworthy that the concomitant bacterial invaders change in kind with advancing age of the young pigs, from Hæmophilus to Pasteurella. The disease cannot be reproduced in its natural form by intranasal inoculation of pigs with artificial mixtures of filtrates derived from affected lungs and cultures of the concomitant organisms grown on laboratory media. It would seem that the bacteria lose their capacity to act in concert with the virus when they have been grown outside the body on culture media. The horse disease investigated by Waldmann and Köbe is, they believe, identical with forms of respiratory affection that have been described under various names in the literature, and they consider that it may assume the clinical picture of an infectious bronchopneumonia, which again has gone under various names, when the requisite secondary bacterial flora are to hand to supplement the action of the virus. They believe it is different, however, from the two great classes of equine respiratory disease—*influenza catarrhalis* and *influenza pectoralis*—that have already been been discussed in this paper. It is worthy of mention that Lührs failed to infect pigs with the bronchial exudate derived from the latter (*brustseuche*) class of disease, these exudates proving, nevertheless, highly virulent to young horses by intranasal application.

To revert, in conclusion, to the work last recorded by Lührs upon the German official investigations into *brustseuche*—we may be allowed perhaps at this stage in the progress of influenza research, to take under review the important findings upon the immunization of horses communicated by him in the light of the recent statements bearing upon the same aspect of the problem that have been made by the workers at Hampstead, dealing with the immunity reactions of the ferret to their strains of presumed human influenza virus, and by Shope, dealing with the immunity reactions of the pig to the American swine influenza virus.

With all three viruses—human, horse and pig—we have, from the recorded evidence, agents which are only capable of producing overt disease when they are implanted upon the respiratory mucosa of a susceptible host. In their natural hosts, their pathogenic action may become greatly enhanced by the supervention of secondary bacterial invaders, to produce a composite and variable clinical disease picture. When these viruses are introduced into the body parenterally, i.e. in any way other than by implantation on the respiratory mucosa, they fail to set up any clinically recognizable disease, but the animals so inoculated are afterwards more or less resistant to natural attack of disease. This has been proved to be the case with the horse and pig, and observations pointing to similar conclusions have now been recorded in ferrets subjected to experiment with the human disease. Although the immunity brought about may not be of very long duration, it is likely that it can be freshened-up by repeated parenteral inoculation with the live virus. Attempts at protection against the natural disease by inoculation with products derived from the secondary bacterial invaders have failed both in horses and pigs.

One may be over-sanguine at this stage in expressing the hope that the means are probably now forthcoming for protection of the human subject in an analogous manner. The work of the Hampstead team has shown that ample virus can be obtained, for any system of immunization of the kind envisaged, from ferrets, which suffer severely from the " clean " virus disease (if, as is most likely, the virus contained in them is actually that of human influenza).

REFERENCES

BEMELMANS, E., *Rev. Gén. Méd. Vét.*, 1921, xxx, 377 (also for literature on equine infectious pneumonia).
    GAFFKY, *Ztschr. f. Veterinärkunde*, 1912, xxiv, 65-76, 113-122, 161-176, 223.
    GAFFKY and LÜHRS, *ib.*, 1913, xxv, 1.
    KÖBE, K., *Deutsche tierärztl., Wchnschr.*, 1934, xcii, 603 (Swine influenza in Germany and literature).
    LÜHRS, "*Festschrift Eugen Fröhner, zusammengestellt von R. v. Ostertag*," 1928, 184-225, Ferdinand Enke, Stuttgart.
    McBRYDE, C. N., NILES, W. B., MOSKEY, H. E., *Journ. Amer. Vet. Assoc.*, 1928, lxxiii, 331.
    SHOPE, R. E., *Journ. Exper. Med.*, 1932, cvi, 575 (Immunity to Swine Influenza).
    THEILER, A., *7th and 8th Repts. Director of Vet. Research, Union of S. Africa*, 1918, 361-393.
    VECHIU, *Rev. Gén. Méd. Vét.*, 1926, xxxv, 241 (also literature on "pink eye").
    WALDMANN, O., and KÖBE, K., *Zbl. Bakt.*, I Abt., Orig., 1934, cxxxiii, 49 (Infectious Bronchitis in Horses).
    Id., *Berlin tierärztl. Wchnschr.*, 1935, li, 2 (Infectious Bronchitis in Cattle).
    WILLIAMS, A. J., *Vet. Record*, 1915, iii, 221.
    ZWICK, W., in "*Kolle, Kraus, and Uhlenhuth's Handb. d. path. Mikroörganismen*," 1929, ix, 413-422 (*Pferdestaupe*) and 423-440 (*Brustseuche*) (literature on equine respiratory diseases).

Dr. E. Stolkind said that while studying in various countries he had seen epidemics of influenza in man at all seasons of the year. Until the virus (or microbe) of influenza was known, only a clinical diagnosis could be made. The most characteristic symptoms of influenza were those of fever and catarrhal inflammations of the nasopharynx, trachea, frequently with bronchitis. The clinical picture of the so-called " common cold " was usually the same. In 1910 and later [1 and 2], he (Dr. Stolkind) had described a special form of paratyphoid fever which he proposed to call the influenzal, or respiratory, paratyphoid as clinically it did not differ from respiratory influenza. Bacteriologically, however, the paratyphoid bacillus was found. This form of paratyphoid fever had since been observed by many authors.

1 STOLKIND, E., *Brit. Journ. Child. Dis.*, 1918, xv, 161.
2 ROLLESTON, J., "Acute Infectious Diseases." London, 1929.

Dr. F. A. Pickworth said he would like to ask whether animals with experimentally produced influenza showed gross pathological changes in the nasal sinuses. He asked this question because in human beings influenza was generally accompanied by or followed by nasal sinusitis which in some cases persisted for years.

Dr. Wilson Smith : A point which puzzled me during our earlier work on influenza in the ferret was the fact that in uncomplicated human influenza the general disturbance is so severe and the malaise and depression last for such a long time. This did not seem to fit in with the conception of the virus attack being solely upon the nasal mucosa and nasal sinuses, for at that time we could find no evidence of other tissues being involved in the ferret disease. The nasal mucosa and sinuses may be even more severely involved in the common cold, yet the general disturbance and after-effects are not comparable with those of influenza.

However, we discovered later a method of inoculation of ferrets which led to severe involvement of the lungs and an illness of greater severity. It seems possible therefore that in man the virus may attack not only the nasal sinuses but also the lungs, and it would be most interesting to obtain, if possible, careful clinical and radiological examinations of the lungs of influenza patients at different stages of the disease.

Dr. E. W. Goodall said that in the investigations and discussions on this subject there was one point of very considerable importance which appeared to have been overlooked, and about which he would ask a question. Had clinical or pathological research been directed to the discovery of any disease in animals which, though not clinically resembling influenza in man, yet might be, in a different form,

the equivalent of that disease, just as vaccinia in cows, a disease very different in its outward form from human variola, was due to the same microbic cause as the latter disease?

Mr. R. E. Glover said that he would like to ascertain the views of Dr. Andrewes and his colleagues on a recent article published by Dr. Eichhorn in which it was suggested that there was an immunological relationship between the influenza virus disease of the ferret and dog distemper.

Dr. Andrewes (in reply to Dr. Pickworth) said that ferrets infected with influenza virus had acute inflammatory lesions involving their turbinate bones and their very extensive frontal sinuses.

In reply to Mr. Glover: His co-workers and himself had repeated the experiments recorded by Eichhorn and Pyle,[1] and had obtained entirely opposite results. Ferrets immune to distemper proved to have normal susceptibility to influenza; ferrets immune to influenza had the same susceptibility to distemper as controls.

[1] *Journ. Amer. Med. Assoc.*, 1934, cii, 2082.

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JOINT DISCUSSION No. 3.

Section of Obstetrics and Gynæcology with the Eugenics Society

Chairman—EARDLEY HOLLAND, F.R.C.S. (President of the Section of
Obstetrics and Gynæcology).

[*February* 15, 1935]

DISCUSSION ON THE STERILIZATION OF WOMEN, INCLUDING INDICATIONS (MEDICAL AND EUGENIC), TECHNIQUE AND LEGAL POSITION

Mr. Victor Lack : The possible medical indications for sterilization are so numerous that it would be tedious to attempt to mention them all. I propose, therefore, to consider only the more important ones.

Group I.—Firstly there is a group of diseases which invariably run a downhill course. There may be temporary improvement, or long periods in which the patient's condition remains nearly stationary, but in all the expectation of life is reduced. Amongst these the most notable are chronic rheumatic carditis, chronic nephritis, diabetes, and some nervous diseases, such as disseminated sclerosis. There can be no doubt that in pregnancy in a patient the subject of these diseases there is a serious risk to the life of the mother and a high probability that the disease will be made worse and most of us will agree that sterilization is desirable in these conditions. In some instances it may be possible to allow the patient to have one or more children before sterilizing, in others pregnancy may be completely contra-indicated. In hospital practice one must not forget that the care of the child after birth may throw a considerable strain on the mother and so make her disease worse. In some instances, as for example in a case of disseminated sclerosis, the patient may be quite unable to care for her child, and although, strictly speaking, this is outside our immediate consideration, this point may, in fact, influence us in our decision to sterilize after terminating pregnancy.

Let us consider a case of mitral stenosis. In a slight case with no history of recurrent attacks of endocarditis it may be possible for the patient to produce two or three children without obvious detriment to her cardiac condition. After that she should be advised to have no more, and be instructed in a good contraceptive technique. If this fails, one must decide between hysterotomy and sterilization or full-time labour, followed by sterilization in the puerperium. In mitral stenosis of moderate severity one might advise Cæsarean section at term with sterilization. In

a severe case with history of previous heart failure, hysterotomy and sterilization would probably be the method chosen.

Group II.—In this group are some diseases from which it is theoretically possible for the patient to recover. The common example is pulmonary tuberculosis ; though tubercle elsewhere and hyperthyroidism are other examples. In practice these diseases are really so similar to those in the first group that they may be treated on the same lines, but sterilization will perhaps not be performed quite so readily. A glance at the list of cases will emphasize this point.

Group III.—Mental disease, including epilepsy. Here we come on to more controversial ground, and I feel that it is better to state my own custom in these cases. A patient who has previously had puerperal insanity, without obvious non-recurring cause, should be sterilized after evacuation of the uterus if she becomes pregnant again. Patients with a bad family history who produce mentally deficient children should be sterilized if they desire it.

Whether it is permissible to sterilize a mentally deficient woman after emptying the uterus I must leave to the medico-legal experts to discuss.

Epileptics produce a proportion of mentally unstable children. During pregnancy the frequency of the fits is often increased but, except indirectly, the patient's life can hardly be said to be in danger. Yet I consider that this is one of the conditions that may justify sterilization if the patient wishes it. On one occasion my failure to appreciate this point resulted in an attempt at suicide by the mother, which was only frustrated by good luck and the maximum of medical skill on the part of one of my colleagues.

What is one to say in the lesser cases ? To the patient, e.g. who is terrified of further pregnancies, perhaps after a previous difficult or dangerous confinement, and who threatens suicide ? I consider that if after careful thought by psychiatrists it is decided that termination of pregnancy is justified, then sterilization is permissible if the patient wishes it. Fortunately these cases are very rare, but they are on the border-line and so worth much thought, as it is but a short step to sterilization at the patient's request.

Group IV.—Obstetrical and gynæcological indications : The commonest single indication for sterilization in this group of cases was repeated Cæsarean section for contracted pelvis. After three Cæsarean sections the abdominal wall and uterus are both considerably damaged, and further pregnancies and Cæsarean sections may expose the patient to an appreciable risk ; most surgeons, therefore, offer the patient sterilization after the third operation. This applies to the upper segment operation particularly. Whether the lower segment operation may be repeated more often with safety remains to be seen.

There are very few other indications. Occasionally sterilization may be a justifiable step in the course of an extensive repair to the pelvic floor, especially if this is combined with an operation for ventro-suspension of the uterus. In some parts of the world osteomalacia might be an indication for sterilization.

There are a few patients who repeatedly develop severe toxæmias in pregnancy and fail to produce a viable child. If, in spite of treatment, this happens on several occasions it may justify sterilization.

Group V.—Hereditary diseases : I need only mention this group, as they will be considered more fully under another heading, but there are some transmutable conditions, as hæmophilia and acholuric familial jaundice, which might justify sterilization.

A word as to the time of sterilization. There are few surgeons so enthusiastic as to walk round the medical wards proposing sterilization to all women with incurable diseases, and in fact one generally performs the operation either after evacuation of the uterus—which I have described here as abdominal hysterotomy— or after Cæsarean section. The operation may occasionally be performed soon after a normal delivery if the patient has been more severely upset by labour than was expected. Generally one advises patients with chronic disease about a good contraceptive technique, and only if this fails and induction of abortion becomes necessary does one suggest sterilization.

Table I shows a list of the conditions for which sterilization has been carried out at the London Hospital during the last five years. In some of these an early pregnancy was terminated by abdominal hysterotomy followed by sterilization; in others a Cæsarean section at term preceded the sterilization, and in a few sterilization was carried out alone, usually soon after the natural termination of a pregnancy. In Table II these details are set forth for the commoner indications.

TABLE I.

Indication for sterilization					No. of cases.
Heart disease	...	...	...	...	20
Contracted pelvis	...	...	...	...	19
Chronic nephritis	...	...	...	...	6
Mental disease	...	...	...	...	4
Epilepsy	...	...	...	...	3
Hyperthyroidism	...	...	...	...	3
Bad obstetric history		...	...	...	2
Rheumatoid arthritis		...	...	...	1
Pulmonary tuberculosis		...	...	...	1
Prolapse	...	...	...	...	1
Osteo-malacia	...	...	...	...	1
After colporrhaphy	...	...	...	...	1
Old nephrectomy and *B. coli* pyelitis			...		1
Hyperpiesia	...	...	...	...	...	1
Kyphosis	...	...	...	...	1

TABLE II.

Indication for sterilization			Hysterotomy sterilization	Cæsarean section sterilization	Sterilization
Heart disease	...	...	11	5	3
Contracted pelvis	...	...		20	
Chronic nephritis	...	...	5		1
Diabetes	...	...	1	3	2
Mental	...	...	4		
Epilepsy	...	...	2		1
Hyperthyroidism	...	...	2	1	
Repeated toxæmias	...	...	1		1
Pulmonary tuberculosis		...	1		

Dr. C. P. Blacker : *History of sterilization.*—In the past, this subject has been much bound up with the problem of mental deficiency, though the Brock Committee included in its recommendations several other groups. The Wood Report estimated that in England and Wales there were 300,000 mental defectives, for 100,000—one-third of the total—of whom they recommended that institutional accommodation should be provided. This would have necessitated a quadrupling of the accommodation for defectives available in 1929 under the Mental Deficiency Acts. If, however, the recommendations of the Wood Committee were now carried out, two-thirds of the total estimated number of mental defectives would live in the general community outside of institutions. It was acknowledged by the Board of Control in its Annual Report for 1928 that it was for these that a case for sterilization

could best be made out. Following the publication of the Wood Report, much interest became centred in the legalizing of voluntary sterilization. But many political and social organizations, puzzled by the conflict of evidence as to heredity, postponed expressing an opinion until the matter had been authoritatively investigated. Finally, in response to a deputation of representatives of three important associations, the Minister of Health appointed a departmental committee under the chairmanship of Mr. L. G. Brock, Chairman of the Board of Control. The report of this committee, which came to be known as the Brock Committee, was published in January 1934.

Racial results obtainable.—The Brock Committee opposed the principle of compulsory sterilization, but recommended that voluntary sterilization, strictly safeguarded, should be available for the following three categories of people:—

(*a*) Persons who are mentally defective or who have suffered from mental disorder.

(*b*) Persons who suffer from, or are believed to be carriers of, grave physical disabilities which have been shown to be transmissible.

(*c*) Persons who are believed to be likely to transmit mental disorder or defect.

The Report, being authoritative and unanimous, exercised a considerable influence on public opinion. The Brock Committee reported on an investigation of the children of 3,733 mentally defective parents, mostly women, of whom no less than 66% were unmarried. These women had had 8,841 children, of whom 22·5% had died—a high mortality rate. Approximately 45% of the children of these mentally defective parents were either themselves mentally defective or mentally retarded and only about 1% were regarded as superior. Most authorities now hold the view that most cases of mental deficiency are the product, in general, of genetic, rather than purely environmental, causes—in other words, that primary aments outnumber secondary. Dr. A. F. Tredgold's estimate that 80% of mental deficiency was "primary" has been much quoted. But by no means all of the 80% have parents one or both of whom are mentally defective. In fact, it is widely held that not more than 5% of the parents of defectives are themselves certifiable as defective. This is a very important figure, because it implies that, if a generation ago, all mental defectives in the country had been prevented from breeding by sterilization or, indeed, by any other method, the reduction in the incidence of mental deficiency would not amount to more than about 5%. Careful perusal of the literature, however, shows that investigations into the ancestry of mental defectives have been carried out with very varying degrees of thoroughness. The more thorough the investigation of the parents, the higher is the proportion found to be certifiable (but not necessarily certified) as mentally defective. No one in this country, however, had proposed compulsion. Voluntary sterilization would, to begin with, be sought by only a small proportion of those persons for whom it might be regarded as an appropriate measure. In the first years of its application, the racial results, so far as mental defectiveness is concerned, would be inappreciable ; in proportion, however, as our knowledge of heredity increased, as a eugenic conscience spread throughout the community, and as the misconceptions about the identity of sterilization with castration were dissipated, so might its practice be extended with more fruitful results. We should be careful how we interfere with human reproductive processes. It is better to start cautiously and feel our way forward than hurriedly to adopt drastic legislation much of which might have to be repealed at a later date.

The subject of the inheritance of mental diseases was left to Dr. A. J. Lewis, the first authority upon it in this country. The subject of hereditary diseases and defects of a physical kind was much too large to deal with in the time available.

Voluntary versus compulsory measures.—All must have come in contact with persons and families concerning whom they felt that compulsory sterilization might

be appropriate. But the advantages of formulating a law with compulsory clauses to cover such persons would be small in comparison with the disadvantages. A drastic sterilization law came into effect in Germany in January 1934, containing both compulsory and voluntary clauses. Nine morbid conditions—including chronic alcoholism—were specified in this Act and were held to justify compulsory sterilization. Any practitioner in Germany, encountering a person for whom a diagnosis was made of one of these nine conditions, was required to notify the case to the authorities. As a result of this, various complications had arisen. Much research has been done in Germany on the inheritance of mental disorders. Such research depends primarily on the submission of truthful pedigrees. If a person felt that by telling the truth about matters concerning his family, he would become a subject for compulsory sterilization, he would conceal essential facts. People were, moreover, reluctant to enter institutions for the treatment of mental disorders, lest one of the dreaded diagnoses should be made and the operation carried out. In this way, the treatment of mental disease has been obstructed in Germany. A slur was, moreover, cast upon the operation of sterilization by its compulsory application. This deterred people from seeking it voluntarily.

In the United States of America, twenty-seven States had passed sterilization laws, and in only one of them (Vermont) was the measure purely voluntary. Yet it appeared that from 80% to 90% of the sterilizations in the United States of America were voluntarily sought. In England, moreover, where sterilization was strongly objected to by people of certain religious denominations, public opinion would not tolerate its compulsory application to persons who objected on moral grounds. More desirable would be the creation of a eugenic conscience which would prompt people to come forward and apply for the operation when this was appropriate.

Safeguards.—Advocates of voluntary sterilization had to face two camps of critics. On one flank were defenders of the liberty of the subject, who maintained that, like contraception, this was a private matter for the decision of the married couple. Medical certificates and authorizations by Government Departments were, according to these critics, as out of place as they would be if it were desired to practise contraception. In the other camp were those who declared that voluntary measures were but the thin end of the wedge, the thick end of which was compulsory sterilization along the lines of the German law. If sterilization were very easily obtained certain practitioners would set up as specialists in it. If the operation became fashionable, people might flock to such practitioners in order to be sterilized for perhaps frivolous reasons. It was generally agreed that the safest methods of sterilization were irreversible, and it was probably more difficult to restore fertility after sterilization, in the man than in the woman. It was easy, therefore, to imagine that if there were no safeguards, many people, acting on an impulse, might get themselves sterilized only to regret it deeply at a later stage in their lives. The Brock Committee had recommended that the candidate's application, backed by two medical certificates, should be submitted to the Minister of Health who, guided by a small Advisory Committee, would have power to authorize or veto the operation. The sanction of the Minister of Health as a safeguard, in addition to two independent medical certificates, had been criticized, but the Brock Committee had submitted good reasons for advocating this measure.

Mr. Cecil Binney (Barrister-at-Law): There is no law directly forbidding sterilization, but it does not follow from this that sterilization is necessarily legal. There can be no doubt, however, that a sterilizing operation, if carried out for the preservation of the patient's health, is, like any other operation, so performed, perfectly legal.

Obviously, to sterilize a person against his will must constitute a crime. That is self-evident. From this one may proceed to consider whether sterilization falls into the category of acts *prima facie* illegal, which are permissible, if done with the patient's consent. For example, of the two most serious " offences; against the person" forbidden by the Act of 1861—murder and rape—murder is an offence, notwithstanding the consent of the person killed. A man may not kill himself and so he may not authorize another to kill him. Thus a surgeon, who put an incurable patient out of his misery at his request, would be guilty of murder, notwithstanding the excellence of his motives. But, if the same surgeon permitted himself to be seduced by a female patient, however immoral his conduct, he would be guilty of no crime, for to an indictment for rape the consent of the woman would be a complete answer. Applying these same principles to the sections of the Act which might cover a surgical operation, there is no doubt that to an indictment for "maiming," or, as lawyers call it, "wounding with intent," consent is no defence; castration certainly falls within this section of the Act. On the other hand, the slightest operation, even removing a patient's clothes without her consent, is a technical assault, but to this charge consent is a complete answer. Intermediate in gravity are the offences of "unlawful wounding" and "an assault occasioning actual bodily harm." A good deal of discussion on the law regarding sterilization has been terminated by a recent decision of the Court of Criminal Appeal to the effect that to neither of these charges is consent a defence. As it does not seem possible to sterilize a person without inflicting some wound, however slight, sterilization would appear to be an act forbidden by the law, except in so far as there might be held to be lawful excuse. For, just as killing a person is not always murder—it may be a pure accident—so all wounding is not unlawful. There can be no doubt that it is lawful to sterilize a person for the sake of his health, just as any other necessary surgical operation is lawful, even though it involves maiming the patient. Equally certainly it would not be regarded as lawful excuse for sterilizing a woman, that she thought that she might lead a more pleasant life after the operation. An operation on eugenic grounds is an intermediate case. It might be held that eugenic considerations made the act lawful, but I incline to the view that it would not be—not because the law has any prejudice against eugenics, but because it will not usually look so far into the ulterior results of an act *prima facie* criminal.

It is possible too, that sterilization may be unlawful, however performed, not because it involves an offence against the person, but because it, in fact, sterilizes. It is not generally known—and how far such a state of the law is desirable is another question—that the Courts can, in effect, create new crimes by treating certain acts as tending to a public mischief contrary to the common law. Only a few years ago a new crime of giving false information to the police as to a supposed robbery, was thus created. It is a question for the judge whether any particular act tends to a public mischief. One cannot, therefore, be certain that sterilization might not in this way be contrary to the criminal law, unless one feels sure that no judge would consider that it tended to the public mischief.

So far as mental defectives or lunatics are concerned, the law seems clear. Since to sterilize a person without his consent is a crime, it must be a crime to sterilize a person who has not the intelligence to consent. It is true, that such persons are not deemed by law entirely incapable of understanding—for example the will of a certified lunatic is not *ipso facto* void—but for practical purposes it is clear that no one will run the risk of sterilizing such a patient. It is possible, moreover, that to perform an operation on one, other than for reasons of health, would constitute an offence under the appropriate sections of the Lunacy Acts and the Mental Deficiency Acts, forbidding the "ill-treatment" of such persons.

To sum up, therefore, a sterilizing operation may be lawfully performed for the patient's health. To perform one without adequate reason is most probably an offence; whether to perform one for eugenic reasons is forbidden or not remains doubtful, except that in the case of lunatics and mental defectives it is illegal.

Mr. V. B. Green-Armytage: A reliable technique for tubal sterilization has been the objective of surgeons for years. Many methods have been tried out by all of us and I think I am right in saying that every one of us has from time to time been disappointed. Indeed, it has been said that hysterectomy is the only really safe procedure, but I may remind you of the fact that extra-uterine pregnancy in the tubes has been recorded after vaginal hysterectomy. That, however, was in France after five years of war.

I have been asked to recount and criticize those methods commonly in use.

Apart from X-rays and the somewhat uncertain biochemical method of injecting, intramuscularly, fresh semen of the husband, the modes of sterilization may be divided into temporary and permanent.

Temporary methods.—Many operations have been devised for temporary occlusion of the tubes but there can be no question that the method which I shall now describe is the simplest and best. The principle depends upon mobilizing the terminal inch of the Fallopian tubes and then, making use of the technique employed when transplanting ureters into the bowel, sliding the freed ends of each tube into letter-box slits previously made in the broad ligament 1 to 2 in. external to the round ligament. Fine catgut is then used to close loosely the openings and the operation is completed.

The technique is simple and bloodless, but care should be taken that the vascular supply of the distal end of the tubes is not disturbed, and that no tension exists.

The advantages of this operation are obvious, for being only of a temporary nature, it compromises no religious ethics, moreover it gets over those psychological inhibitions which so often confront us, wherein a woman refuses to be permanently unable to conceive. Another advantage is to be found in the fact that in the event of remarriage the buried but functionally healthy portion of the tube can be made free again. Many instances of such freedom being followed by pregnancy have been recorded.

Permanent methods.—Every surgeon has a preference for some particular device, some are good, others are indifferent; time and experience will occasionally manifest the extraordinary regenerative capacity of the tubal epithelium, and compel him to change his technique.

Method 1.—Simple ligation with thread or silk, without cutting out a portion of the tube, is only mentioned to be condemned as useless.

Method 2.—The Madlener technique of crushing one inch of the tube and its immediate mesosalpinx and then tying a double loop of thread, has many advocates, but in a small percentage lipiodolograms at a later date have shown that the oviduct has reconstructed itself under the ligated area.

Method 3.—Ligation in two places and resection of an intervening inch, with touching of the cut ends of the tubes with pure carbolic or actual cautery, is very frequently successful—probably in more than 90% of cases, but such a method can be improved upon, either by riding and plicating one tube over the other as in fig. 4, or by burying each cut end in separate compartments of the broad ligament.

Method 4.—Salpingectomy is as nearly foolproof, or ovum-proof, as is possible. The essential part of the operation is the removal of a wedge of the tube at the uterine cornu; Lembert catgut sutures are then employed on a non-cutting needle. The whole raw surface from which the tube has been removed being peritonealized.

Method 5.—Recently an American surgeon, J. M. Slemons, has modified the above technique by transplanting the divided uterine ends of the tubes (after deep cornual resection of the isthmial portions) into a stab incision on the anterior surface of the body of the uterus. If care is taken to obtain complete hæmostasis this method seems to have many advantages and is one which I intend to put into practice.

The above methods are, of course, by the abdominal route and present no difficulty. There are, however, many women who are averse to laparotomy even though the appendix can be removed or the uterus slung up at the same time ; for this reason many years ago I devised a technique which is simple and secure in 99% of cases, a technique which can be performed in the nullipara or in those who have had children. It can be performed, if need be, as part of the operation, when a reputable physician requests that pregnancy should be terminated in the first few weeks on account of such diseases as tuberculosis, morbus cordis or epilepsy.

The operation briefly consists in opening the utero-vesical pouch per vaginam, the bladder being retracted. By the use of two "catspaws" the uterus is anteverted and brought down. If the vagina is patulous there will be no difficulty in delivering the fundus of the uterus through the opening in the utero-vesical pouch. This being done, the cornual end of each tube can be excised and sewn over ; the cut distal portion being buried and peritonealized—a matter of a few moments. The uterus is replaced, the cut edges of the peritoneum are sewn and the vaginal incision is closed.

In the event of a nullipara when tightness of the vagina makes exposition of the fundus almost impossible, I use the catspaws as before, and then with sponge-holding forceps bring down a loop of the Fallopian tube one side at a time. I ligate the oviduct in two places with thread and resect one inch, touching each cut surface of the tube with pure carbolic or a diathermy needle. The cauterized ends are then either allowed to slip back—as some surgeons allow the stump of the appendix to slip back—or the ends are plicated or buried.

This technique I have employed on many scores of occasions, and it is one that I can highly recommend, for, apart from the fact that it is successful in 99% of cases, it is inexpensive and time-saving, it has no after-complications, there is no pain, and the patient is up and about after one week, with no abdominal disability.

Dr. Aubrey Lewis, dealing with the importance of the psychiatric aspects of sterilization, said that the therapeutic indications were to be found in a study of the individual case rather than in any general rules. In the case of puerperal psychoses it had been shown, for example, that the majority of these represented an isolated happening in a series of normal pregnancies and confinements, though in a small number of patients there was a considerable likelihood of recurrence which could be recognized in advance. Similarly, individual study was called for in eugenic matters. Although there were large statistics available as to the inheritance of various mental disorders, the conclusions could not be applied out of hand to a particular patient ; the diagnosis alone was not sufficient to indicate the genetic probabilities. One was dealing for the most part with illnesses in which the environment played no small part in bringing the inherited proclivities to manifestation. By a careful study, however, of any patient's antecedents, personal history, and illness, one could arrive at a more confident genetic prognosis. There was also to be considered what good points there were in the patient's transmissible endowment ; one had to balance these against the morbid taints. Sterilization was not applicable to every patient who had had an attack of mania or morbid depression, irrespective of his other qualities.

He agreed with Dr. Blacker's opinion that a sound eugenic conscience ought to be fostered among the public. An increasing number of people who attended such a hospital as the Maudsley spontaneously asked for guidance on these matters; sometimes it was a relative or fiancée who raised the issue. Dr. Blacker had spoken of safeguards; they were necessary for the patient and for the doctor. A minority of patients who asked about sterilization did so because of morbid fears, or sought it for frivolous motives; in their own interests they must be reassured and deterred by conscientious expert advice. Rarely also it might happen that a patient afterwards resented the sterilization carried out at her own wish and for good medical reasons. He emphasized the need for the surgeon in such a case to be exempt from any anxiety as to legal penalties.

Dr. B. Dunlop said that he was a medical member of the Eugenics Society, but had always expressed misgivings about its sterilization policy. He feared that a Bill merely to legalize eugenic sterilization would have the effect of making sterilization on economic grounds illegal. He held it to be urgently needed that poor people who had already as many children as they could provide for, and who found the ordinary methods of contraception too inconvenient or expensive, should be able to get sterilized; and advocated that the operation should be available to any person with two children. Moreover, this would gradually solve the "carrier" problem, whereas it was very doubtful if Parliament would pass a purely eugenics Bill including this most important point, notwithstanding the recommendation of the Brock Committee Report. He deprecated the hesitation expressed by one of the speakers about sterilizing seriously diseased women if they had only two or three children, because this attitude towards the unfit and the poor added greatly to the financial burden which prevented many thousands of middle-class people of good stock getting married or else having adequate families.

Dr. K. B. Aikman said that he disagreed with Dr. Dunlop. Speaking as a member of the Council of the Eugenics Society and also of the Committee for Legalizing Voluntary Eugenic Sterilization, he knew that both were convinced advocates of legal safeguards. They were supported by experience in the United States, where lack of safeguards allowed some frivolous sterilizations, tending to damage the movement. The recent trial at Graz, Austria, also confirmed this view. There, many male sterilizations, merely for birth control and not for eugenics, had been held contrary to the public interest and the operators were severely punished.

Captain Pitt-Rivers: The eugenic approach to the problem of surgical sterilization necessarily differs from the medical approach. Medical considerations are restricted to the health of the individual and do not deal with points of social ethics. Further, the physician is debarred from considering the moral and ethical claims of the individual in so far as these moral claims conflict with the law.
Were the law to recognize the individual's right to control his or her functions of reproduction, and society's right to control the reproduction of healthy stock in its own interests, medical and gynæcological indications for sterilization for contraception, and for the termination of pregnancy, would conform to the patient's desires. Unwanted pregnancy cannot be in the interests either of an individual woman or of society. From the point of view of society, protection and encouragement of unwanted pregnancies can lead only to an increase in illegitimate births, self-induced and dangerous abortions, undesirable marriages, and

defective stock.   The present state of the law encourages these results—undesirable from both the individual and the social point of view.

What are at present held to be medical and gynæcological indications for sterilization, for the termination of pregnancy, and for contraceptive advice are in reality false theological and ethical intrusions—in short they are humbug.

What is advocated as "voluntary" sterilization, is not so, so long as so-called medical "safeguards" are demanded.   The physician is not competent to pronounce upon either eugenic indications or the individual's right to control her own bodily functions and should no more be involved than when a female patient requests a surgeon to perform a "face-lifting" operation.

In Germany applications for voluntary sterilization (unsupported by judicial decision in the special Courts) are refused, while compulsory sterilization has, it is alleged, been ordered, against the individual's wishes, in cases of traumatic epilepsy where there are no genetical indications in the pedigree.

In England legislative reform should take the form of legalizing strictly voluntary sterilization with special provision for dealing with certifiable mental defectives, whilst medical interests should be restricted to clinical matters.   The surgeon's freedom to carry out his patient's wishes should therefore be protected.

Dr. S. K. Westmann: The voluntary and compulsory sterilization now introduced in Germany is carried out in cases of : (1) Innate mental deficiency ; (2) manic-depressive insanity ;   (3) schizophrenia ;   (4) hereditary epilepsy ; (5) Huntington's chorea ;   (6) hereditary blindness ;   (7) hereditary deafness ; (8) severe hereditary deformities ; (9) severe alcoholism.

The sterilization "may" be performed on voluntary application of the deficient himself or of the persons in charge of him and "has" to be performed on decision of the respective courts ("Erbgesundheitsgerichte ").

The operation consists—in the male, of a vasotomy ; in the female, of a salpingotomy.   It is prohibited to use rays or chemical remedies.   Also castration is forbidden.   The German authorities advise the operation described by Döderlein (formation of a knot of the Fallopian tubes and securing it by means of catgut sutures).

According to the official publications, the number of congenitally mentally deficient persons averages 1% of the whole population.   From 33% to 50% of the children of these persons are again mentally deficient and it is proved that the apparently healthy remainder inherit the disposition and are liable to pass it on to their descendants.

In the asylum of the City of Berlin (Wittenau) 58·1% of the imbecile children had one parent, and 72% both parents, mentally defective.

As the experiment of sterilization on a large scale in Germany is in its earliest stage, it seems advisable to wait for the result in that country before giving any definite opinion.

Mr. Aleck Bourne described a method of sterilizing women, which he was testing—by cauterizing the uterine openings of the Fallopian tubes.   He used a diathermy electrode—curved to adapt itself to the shape of the lateral wall of the uterine cavity—which could be passed after dilatation of the cervix to the size of No. 6, Hegar's dilator.

The electrode was passed until its point, $\frac{1}{8}$ in. in diameter, was felt to rest in the cornual angle.   The current was turned on, and the uterine tissue of the region of the tubal orifice was then deeply burned for about twenty seconds on both sides.

The operation could be carried out under gas or evipan, and could be completed in five minutes.

From six weeks to two months after the operation the patient was examined by X-rays during lipiodol injection of the uterus, and again twenty-four hours after the injection, in order to test the occlusion of the tubes.

[Mr. Bourne showed some X-ray photographs of the lipiodol shadow. The first cases were failures as demonstrated by the percolation of lipiodol into the tubes ; two films showed a haziness of the cornual angles suggesting that the openings were not completely occluded, while the last case operated upon gave films which showed complete occlusion by the sharp rounded outline of the tubal angles of the uterus.]

After recent practice with the electrode, he considered that the method would prove sufficiently certain to justify its adoption.

Dr. Leonard Findlay said he agreed with Dr. Blacker that it was unfortunate that the question of sterilization had centred to such an extent on that of mental deficiency. Hence he was astonished that Dr. Blacker in his arguments for sterilization had himself used almost entirely this very condition. He thought that Dr. Blacker would have made out a much better case if he had concentrated on such diseases as deafmutism, hæmophilia, and the muscular dystrophies which were universally admitted to be hereditary in nature. On the other hand there was the gravest doubt if what was called mental deficiency—and certainly if what was considered by the man in the street and the profession at large as mental deficiency— was hereditary. In this question much confusion had arisen from the assumption that all mental deficiency was merely a matter of deficient intelligence, and that it was thus permissible in any analytical study to combine high- and low-grade mental deficiency as well as insanity. Intelligence, as such, was undoubtedly hereditary and much of the high-grade mental deficiency was simply an expression of the natural variation in intelligence. In this type of the mischief deficient intelligence was the sole abnormal feature, and when analysed by itself revealed a strong hereditary tendency. But in the case of low-grade mental deficiency, impairment of intelligence in a large proportion of the patients was only one of the abnormal features. There were, e.g. bodily deformities in the mongolian type, and paralyses of various grades in the spastic diplegics and hemiplegics. This fact surely showed that these various types were different conditions and thus were almost certainly dependent on different causes. Consequently they should be grouped apart, and it was, without doubt, because of the neglect of this precaution, and because of the very varying proportions of high- and low-grade cases in any group, that statistics from various sources showed such different estimates of the hereditary factor as $6 \cdot 6$ and $56 \cdot 6\%$. In the Brock Report, for example, any child, irrespective of its age, who was two years retarded educationally was considered mentally defective. There was all the difference in the world between this degree of retardation at 6 years and the same degree at 12 years of age, and hence such a grouping was bound to combine simply backward children with true mental defectives and, depending on the proportion of the former, would reveal a strong or a weak hereditary history.

Again, no one believed that all low-grade mental deficiency was hereditary. No one, for example, believed that mongolian idiocy was hereditary. Further, there were the examples due to disease and injury at birth. Hence it was important to have some idea of the relative incidence of the various types of mental deficiency in order to form an estimate of the problematical effect of sterilization. In this connexion he recalled the thorough clinical investigation on this question conducted by Dr. John

Thomson. He (Dr. Findlay) had himself just completed an analysis of the examples of mental deficiency which he had seen in private practice over a period of twenty years, and which revealed the same relative incidence as did the analysis of Dr. Thomson. Roughly, 30% were examples of amentia, 30% were mongols, and 30% were cases of spastic diplegia and hemiplegia, so that he had a difficulty in seeing where the 80% of primary amentia usually referred to came from, the elimination of which was suggested to the public as the probable benefit from sterilization.

In conclusion :—He was not impressed by the reasons given for voluntary as against compulsory sterilization. It seemed to him that the class in which it would be most productive of good—namely: the high-grade defective or mentally backward—was the very class in which the idea of voluntary sterilization would not be entertained, as the individuals forming this class were, as a rule, quite pleased with themselves and their stock.

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